```
=> fil reg; d ide l9
FILE 'REGISTRY' ENTERED AT 13:00:21 ON 17 JUN 2003
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STRUCTURE FILE UPDATES:   16 JUN 2003  HIGHEST RN 532194-47-1
DICTIONARY FILE UPDATES:  16 JUN 2003  HIGHEST RN 532194-47-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf


L9   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   178167-88-9  REGISTRY
CN   2H-1-Benzopyran-2-propanoic acid, 3,4-dihydro-6-hydroxy-2,7,8-trimethyl-,
     (2S)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   2H-1-Benzopyran-2-propanoic acid, 3,4-dihydro-6-hydroxy-2,7,8-trimethyl-,
     (S)-
OTHER NAMES:
CN   (S)-LLU-.alpha.
CN   Natriuretic agent LLU-.alpha.
CN   Natriuretic factor LLU-.alpha.
FS   STEREOSEARCH
DR   170427-25-5
MF   C15 H20 O4
SR   CA
LC   STN Files:   CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry.
```
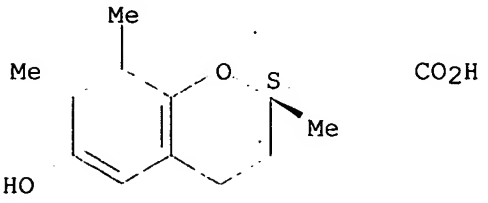

chroman derivative

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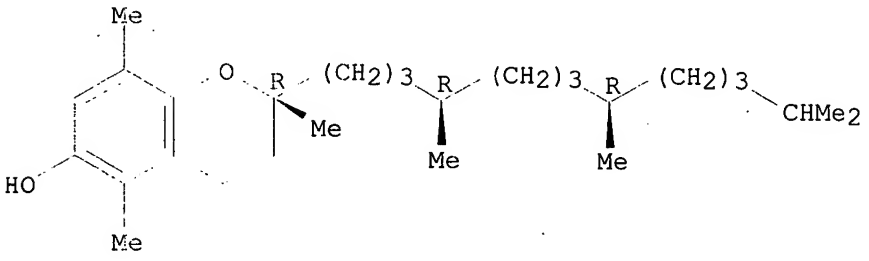
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

              19 REFERENCES IN FILE CA (1957 TO DATE)
              19 REFERENCES IN FILE CAPLUS (1957 TO DATE)


=> d ide l10; d ide l11; d ide l12
```

L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 148-03-8 REGISTRY
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,5,8-trimethyl-2-[(4R,8R)-4,8,12-trimethyltridecyl]-, (2R)-rel- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,5,8-trimethyl-2-(4,8,12-trimethyltridecyl)-, [2R*(4R*,8R*)]-
CN 6-Chromanol, 2,5,8-trimethyl-2-(4,8,12-trimethyltridecyl)- (8CI)
OTHER NAMES:
CN **.beta.-Tocopherol**
CN 2,5,8-Trimethyl-2-(4,8,12-trimethyltridecyl)-6-chromanol
CN 5,8-Dimethyltocol
CN Cumotocopherol
CN DL-.beta.-Tocopherol
CN dl-.beta.-Tocopherol
CN Neotocopherol
CN p-Xylotocopherol
FS STEREOSEARCH
DR 16662-70-7
MF C28 H48 O2
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MRCK*, NAPRALERT, PROMT, SPECINFO, TOXCENTER, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Relative stereochemistry.



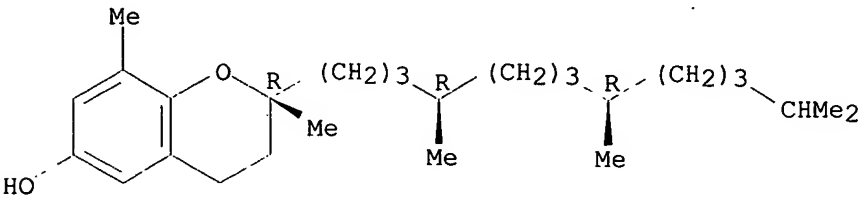
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1185 REFERENCES IN FILE CA (1957 TO DATE)
27 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1188 REFERENCES IN FILE CAPLUS (1957 TO DATE)
10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L11 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 119-13-1 REGISTRY
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,8-dimethyl-2-[(4R,8R)-4,8,12-trimethyltridecyl]-, (2R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,8-dimethyl-2-(4,8,12-trimethyltridecyl)-, [2R-[2R*(4R*,8R*)]]-
CN 6-Chromanol, 2,8-dimethyl-2-(4,8,12-trimethyltridecyl)- (8CI)

OTHER NAMES:
CN (+)-.delta.-Tocopherol
CN (2R,4'R,8'R)-.delta.-Tocopherol
CN (R,R,R)-.delta.-Tocopherol
CN .delta.-D-Tocopherol
CN **.delta.-Tocopherol**
CN .delta.-Vitamin E
CN 8-Methyltocol
CN d-.delta.-Tocopherol
CN D-.delta.-Tocopherol
CN E-Mix D
FS STEREOSEARCH
DR 16698-36-5, 78656-14-1, 37816-35-6
MF C27 H46 O2
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MRCK*, NAPRALERT, PROMT, TOXCENTER, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1523 REFERENCES IN FILE CA (1957 TO DATE)
25 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1525 REFERENCES IN FILE CAPLUS (1957 TO DATE)
10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

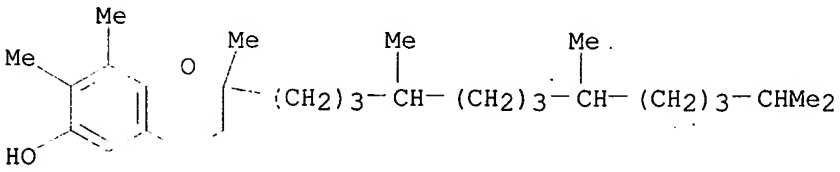
L12 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 7616-22-0 REGISTRY
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,7,8-trimethyl-2-(4,8,12-trimethyltridecyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6-Chromanol, 2,7,8-trimethyl-2-(4,8,12-trimethyltridecyl)- (8CI)
OTHER NAMES:
CN **.gamma.-Tocopherol**
CN .gamma.-Tokoferol
CN 7,8-Dimethyltocol
CN dl-.gamma.-Tocopherol
CN DL-.gamma.-Tocopherol
CN o-Xylotocopherol
FS 3D CONCORD
DR 7540-59-2, 119-11-9
MF C28 H48 O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,

BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CHEMLIST, CIN, DDFU, DETHERM*, DRUGU, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MRCK*, NAPRALERT, NIOSHTIC, PIRA, PROMT, SPECINFO, TOXCENTER, USPAT2, USPATFULL, VETU

(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2296 REFERENCES IN FILE CA (1957 TO DATE)
33 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2299 REFERENCES IN FILE CAPLUS (1957 TO DATE)

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=> fil capl; d que 15; d que 117
FILE 'CAPLUS' ENTERED AT 13:02:21 ON 17 JUN 2003
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FILE COVERS 1907 - 17 Jun 2003  VOL 138 ISS 25
FILE LAST UPDATED: 16 Jun 2003  (20030616/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
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Inventors

```
L1          3287 SEA FILE=CAPLUS ABB=ON  MILLER G?/AU
L2          2758 SEA FILE=CAPLUS ABB=ON  BROWN L?/AU
L4         72355 SEA FILE=CAPLUS ABB=ON  ?ISCHEM? OR CYTOPROTECT?
L5             5 SEA FILE=CAPLUS ABB=ON  L1 AND L2 AND L4


L1          3287 SEA FILE=CAPLUS ABB=ON  MILLER G?/AU
L2          2758 SEA FILE=CAPLUS ABB=ON  BROWN L?/AU
L9             1 SEA FILE=REGISTRY ABB=ON  178167-88-9/RN
L13           19 SEA FILE=CAPLUS ABB=ON  L9
L17            0 SEA FILE=CAPLUS ABB=ON  (L1 OR L2) AND L13


=> fil medl; d que 133; d que 167

FILE 'MEDLINE' ENTERED AT 13:02:21 ON 17 JUN 2003

 FILE LAST UPDATED: 14 JUN 2003 (20030614/UP).  FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L31         2510 SEA FILE=MEDLINE ABB=ON  MILLER G?/AU
L32         2404 SEA FILE=MEDLINE ABB=ON  BROWN L?/AU
L33            0 SEA FILE=MEDLINE ABB=ON  L31 AND L32


L31         2510 SEA FILE=MEDLINE ABB=ON  MILLER G?/AU
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```
L32        2404 SEA FILE=MEDLINE ABB=ON  BROWN L?/AU
L36       35432 SEA FILE=MEDLINE ABB=ON  HYPOXIA-ISCHEMIA, BRAIN+NT/CT
L37         183 SEA FILE=MEDLINE ABB=ON  SPINAL CORD ISCHEMIA+NT/CT
L67           7 SEA FILE=MEDLINE ABB=ON  (L31 OR L32) AND (L36 OR L37)


=> fil embase; d que 174; d que 176; d que 184

FILE 'EMBASE' ENTERED AT 13:02:22 ON 17 JUN 2003
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 FILE COVERS 1974 TO 12 Jun 2003 (20030612/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L64        1753 SEA FILE=EMBASE ABB=ON  MILLER G?/AU
L65        1720 SEA FILE=EMBASE ABB=ON  BROWN L?/AU
L74           0 SEA FILE=EMBASE ABB=ON  L64 AND L65



L9            1 SEA FILE=REGISTRY ABB=ON  178167-88-9/RN
L10           1 SEA FILE=REGISTRY ABB=ON  .BETA.-TOCOPHEROL/CN
L11           1 SEA FILE=REGISTRY ABB=ON  .DELTA.-TOCOPHEROL/CN
L12           1 SEA FILE=REGISTRY ABB=ON  .GAMMA.-TOCOPHEROL/CN
L64        1753 SEA FILE=EMBASE ABB=ON  MILLER G?/AU
L65        1720 SEA FILE=EMBASE ABB=ON  BROWN L?/AU
L72         546 SEA FILE=EMBASE ABB=ON  BETA TOCOPHEROL/CT OR DELTA TOCOPHEROL/
               CT OR GAMMA TOCOPHEROL/CT
L73         546 SEA FILE=EMBASE ABB=ON  (L9 OR L10 OR L11 OR L12)
L76           0 SEA FILE=EMBASE ABB=ON  (L64 OR L65) AND (L72 OR L73)



L64        1753 SEA FILE=EMBASE ABB=ON  MILLER G?/AU
L65        1720 SEA FILE=EMBASE ABB=ON  BROWN L?/AU
L77       27750 SEA FILE=EMBASE ABB=ON  BRAIN ISCHEMIA+NT/CT
L84           5 SEA FILE=EMBASE ABB=ON  L77 AND (L64 OR L65)


=> fil wpids; d que 189

FILE 'WPIDS' ENTERED AT 13:02:23 ON 17 JUN 2003
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FILE LAST UPDATED:          16 JUN 2003      <20030616/UP>
MOST RECENT DERWENT UPDATE:     200338        <200338/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS  <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<
```

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT: http://www.derwent.com/userguides/dwpi_guide.html <<<

L87 804 SEA FILE=WPIDS ABB=ON MILLER G?/AU
L88 358 SEA FILE=WPIDS ABB=ON BROWN L?/AU
L89 5 SEA FILE=WPIDS ABB=ON L87 AND L88

=> dup rem l67,l5,l84,l89

FILE 'MEDLINE' ENTERED AT 13:02:24 ON 17 JUN 2003

FILE 'CAPLUS' ENTERED AT 13:02:24 ON 17 JUN 2003
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FILE 'EMBASE' ENTERED AT 13:02:24 ON 17 JUN 2003

FILE 'WPIDS' ENTERED AT 13:02:24 ON 17 JUN 2003

PROCESSING COMPLETED FOR L67
PROCESSING COMPLETED FOR L5
PROCESSING COMPLETED FOR L84
PROCESSING COMPLETED FOR L89
L102 16 DUP REM L67 L5 L84 L89 (6 DUPLICATES REMOVED)
ANSWERS '1-7' FROM FILE MEDLINE
ANSWERS '8-12' FROM FILE CAPLUS
ANSWERS '13-15' FROM FILE EMBASE
ANSWER '16' FROM FILE WPIDS

=> d ibib ab hitrn 1-16

L102 ANSWER 1 OF 16 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999158519 MEDLINE
DOCUMENT NUMBER: 99158519 PubMed ID: 10051210
TITLE: Regulation of ischemic cell death by glucocorticoids and adrenocorticotropic hormone.
AUTHOR: Antonawich F J; **Miller G**; Rigsby D C; Davis J N
CORPORATE SOURCE: Department of Neurology, SUNY at Stony Brook, NY 11794-8121, USA.
CONTRACT NUMBER: NS 30559 (NINDS)
SOURCE: NEUROSCIENCE, (1999 Jan) 88 (1) 319-25.
Journal code: 7605074. ISSN: 0306-4522.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990511
Last Updated on STN: 20000303
Entered Medline: 19990426
AB Transient global ischemia results in delayed selective neuronal death of hippocampal CA1 pyramidal cells. Glucocorticoids increase and adrenalectomy decreases the rate of neuronal death; however, they also produce changes in brain temperature, serum glucose and adrenocorticotropic hormone levels. In order to understand the role of glucocorticoids in regulating ischemic cell death, we studied RU 38486, a glucocorticoid receptor blocker, and Org 2766, a non-steroidogenic

adrenocorticotropic hormone 4-9 analog. Male Mongolian gerbils were subjected to 5 min of bilateral carotid artery occlusion under a controlled temperature environment (37.0-38.0 degrees C). Animals were injected with either physiological saline, Org 2766 (10 microg/kg/24 h) or RU 38486 (50 mg/kg/8 h), beginning just prior to the occlusion until killing at either day 4 or 7. Blood was collected for serum glucose and cortisol analysis. Damage was evaluated by blinded counts of CAI neurons. Both RU 38486 and Org 2766 treatment significantly (P<0.004) reduced hippocampal CA1 damage at day 4, but not on day 7. While RU 38486 raised serum cortisol and adrenocorticotropic hormone levels, neither treatment affected temperature or serum glucose. The fact that RU 38486 mimicked adrenalectomy without changing temperature suggests that the decreased rate of cell death resulted from either removal of glucocorticoids or increases in adrenocorticotropic hormone. The ability of Org 2766 to affect this rate strongly suggests that adrenocorticotropic hormone is the active regulatory hormone rather than glucocorticoids. While both RU 38486 and Org 2766 prolong the survival of CA1 neurons after transient global ischemia, only RU 38486, which is available and tested in both animals and humans, can block the detrimental effects of post-ischemia glucocorticoid elevations. Thus, the administration of RU 38486 may be a practical adjunct to other neuroprotective agents for victims of cardiac arrest, anesthetic accidents or drowning.

L102 ANSWER 2 OF 16 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 95172198 MEDLINE
DOCUMENT NUMBER: 95172198 PubMed ID: 7867766
TITLE: The interleukin-1 receptor antagonist (rhIL-1ra) protects against cerebral infarction in a rat model of hypoxia-ischemia.
AUTHOR: Martin D; Chinookoswong N; **Miller G**
CORPORATE SOURCE: Department of Pharmacology, Synergen, Inc., Boulder, Colorado 80301.
SOURCE: EXPERIMENTAL NEUROLOGY, (1994 Dec) 130 (2) 362-7. Journal code: 0370712. ISSN: 0014-4886.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950407
Last Updated on STN: 20000303
Entered Medline: 19950327

AB We assessed the cerebral protective effects of the competitive interleukin-1 antagonist rhIL-1ra in 7-day-old rats that were subjected to brain hypoxia-ischemia by unilateral carotid artery ligation and subsequent exposure to 2 h of 7.5% O2-balanced N2. This procedure leads to atrophy in the cerebral hemisphere ipsilateral to carotid occlusion, with prominent foci of neuronal infarction in the striatum. Systemic administration of 100 mg/kg of rhIL-1ra before and/or after the hypoxic exposure limited the insult. The results indicate that rhIL-1ra has potent neuroprotective properties against morphologic brain injury from hypoxia-ischemia. rhIL-1ra may prove to be clinically useful in protecting against hypoxia-ischemia-related disorders.

L102 ANSWER 3 OF 16 MEDLINE
ACCESSION NUMBER: 95122998 MEDLINE
DOCUMENT NUMBER: 95122998 PubMed ID: 7822731
TITLE: Long-term MRI changes in brain after pediatric open heart surgery.
AUTHOR: **Miller G**; Mamourian A C; Tesman J R; Baylen B G; Myers J L
CORPORATE SOURCE: Section of Pediatric Neurology, Baylor College of Medicine, Texas Children's Hospital, Houston 77030.

SOURCE: JOURNAL OF CHILD NEUROLOGY, (1994 Oct) 9 (4) 390-7.
Journal code: 8606714. ISSN: 0883-0738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950223
Last Updated on STN: 20000303
Entered Medline: 19950210

AB We performed magnetic resonance imaging (MRI) on the brain and neurologic examinations on 23 children after open heart surgery for congenital heart disease. Twenty children also had psychometric assessments. Examinations were performed at a mean age of 66 months (range, 26 to 180 months). Age at operation was less than 1 month in 43% and more than 6 months in 45%. Abnormal scans were found in 17 (74%) and showed diffuse findings consistent with hypoxic-ischemic encephalopathy, with or without areas of cortical infarction; focal cortical infarction alone; and (in one patient) callosal agenesis and abnormal neuronal migration. Normal IQ and neurologic examinations were found in all six of those who had a normal MRI, and five of six children with changes consistent with focal cortical infarction without diffuse change had a normal neurologic examination. Cerebral palsy and mental retardation was common in the group with diffuse abnormality (in eight of nine children), and this was more likely to occur in those who underwent prolonged (> 45 minutes) hypothermic circulatory arrest and operation during early infancy (P = .004). Focal cortical findings without diffuse changes were more likely in those who underwent open heart surgery without hypothermic circulatory arrest and were older than 6 months at operation, and these children were less likely to have frank neurodevelopmental sequelae. Thus, in our population, focal cortical lesions were common after open heart surgery, and, in addition, diffuse brain abnormality on MRI plus neurologic sequelae were common after prolonged hypothermic circulatory arrest.

L102 ANSWER 4 OF 16 MEDLINE
ACCESSION NUMBER: 90189966 MEDLINE
DOCUMENT NUMBER: 90189966 PubMed ID: 2179646
TITLE: Right aortic arch with isolation of the left subclavian artery: case report and review of the literature.
AUTHOR: Luetmer P H; **Miller G M**
CORPORATE SOURCE: Department of Diagnostic Radiology, Mayo Clinic, Rochester, MN 55905.
SOURCE: MAYO CLINIC PROCEEDINGS, (1990 Mar) 65 (3) 407-13. Ref: 30
Journal code: 0405543. ISSN: 0025-6196.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW OF REPORTED CASES)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199004
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19900601
Entered Medline: 19900419

AB Of the right aortic arch anomalies, a right arch with isolation of the left subclavian artery is the least common. Herein we describe a 52-year-old woman in whom this anomaly was discovered during cerebral angiography for evaluation of a giant symptomatic intracavernous carotid aneurysm. Isolation of the left subclavian artery may be suggested in a patient with a right arch in whom the blood pressure or pulse in the left upper extremity is diminished. Although the isolated left subclavian artery produces the hemodynamic alterations of a subclavian steal, review of the 39 cases reported in the literature revealed only 5 patients with

symptoms suggestive of vertebrobasilar insufficiency and 5 patients with weakness of the left upper extremity. Although the patient we describe had no known heart disease, congenital heart disease was present in 23 of the 39 reported cases (59%), tetralogy of Fallot occurring most frequently.

L102 ANSWER 5 OF 16 MEDLINE
ACCESSION NUMBER: 86273318 MEDLINE
DOCUMENT NUMBER: 86273318 PubMed ID: 3731809
TITLE: Computed tomography in global cerebral cortical ischemia of the neonate and young infant.
AUTHOR: Swartz J D; Soyer A; **Brown L W**; Faerber E N; Stoutenger W A; Anzil A P
SOURCE: JOURNAL OF COMPUTED TOMOGRAPHY, (1986 Jul) 10 (3) 243-7. Journal code: 7805373. ISSN: 0149-936X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198609
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 20000303
Entered Medline: 19860918
AB The authors have encountered three unique neonates with global cerebral cortical ischemia. The pathogenesis and computed tomography scans of these patients who sustained profound hypoxemia is described. Follow-up computed tomography scans in each case demonstrated generalized loss of cortical substance.

L102 ANSWER 6 OF 16 MEDLINE
ACCESSION NUMBER: 87127767 MEDLINE
DOCUMENT NUMBER: 87127767 PubMed ID: 3545165
TITLE: Persistent hypoglossal artery--a case report.
AUTHOR: **Miller G J**; Sacharias N
SOURCE: AUSTRALASIAN RADIOLOGY, (1986 Aug) 30 (3) 209-12. Journal code: 0047441. ISSN: 0004-8461.
PUB. COUNTRY: Australia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198702
ENTRY DATE: Entered STN: 19900303
Last Updated on STN: 20000303
Entered Medline: 19870227

L102 ANSWER 7 OF 16 MEDLINE
ACCESSION NUMBER: 78014558 MEDLINE
DOCUMENT NUMBER: 78014558 PubMed ID: 906054
TITLE: Three-area epidemiological study of geographic differences in stroke mortality. II. Results.
AUTHOR: Stolley P D; Kuller L H; Nefzger M D; Tonascia S; Lilienfeld A M; **Miller G D**; Diamond E L
SOURCE: STROKE, (1977 Sep-Oct) 8 (5) 551-7. Journal code: 0235266. ISSN: 0039-2499.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197711
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 20000303
Entered Medline: 19771125
AB An epidemiological study was conducted of geographic differences in stroke

mortality between the following areas within the United States; Savannah, Georgia (high stroke rates), Hagerstown, Maryland (intermediate stroke rates) and Pueblo, Colorado (low stroke rates). Population samples 35--54 years of age of the three cities were drawn for interview and examination to determine medical conditions and living habits of these populations. The population samples were compared with emphasis on possible risk factors for stroke: serum cholesterol and glucose tolerance test determinations, weight and height measurements, blood pressure and cigarette smoking. The gradient of increasing prevalence of stroke-related risk factors from low to intermediate to high for the three cities was present for blood pressure in black females and white males and for glucose tolerance tests in whites and nonwhites. No other consistent pattern of increasing prevalence of risk factors for stroke was evident.

L102 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 2003:97274 CAPLUS
DOCUMENT NUMBER: 138:153318
TITLE: Preparation of substituted phenols as **cytoprotective** agents useful in pharmaceutical and cosmetic formulations
INVENTOR(S): Wang, Bing; Zhang, Yong-Kang; Chen, Jian; Zhang, Wei; Song, Jiangao; Del, Balzo Ughetta; **Brown, Lesley; Miller, Guy**
PATENT ASSIGNEE(S): Galileo Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 161 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003009807	A2	20030206	WO 2002-US23509	20020723
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003073712	A1	20030417	US 2002-202670	20020723

PRIORITY APPLN. INFO.: US 2001-307439P P 20010723
US 2002-353702P P 20020131
OTHER SOURCE(S): MARPAT 138:153318
AB Phenolic derivs. having conjugated bonds I [wherein R = NO2, substituted alkenyl, or (un)substituted aryl(carbonyl), heteroaryl, or heterocyclyl; R1-R5 = independently H, carboxy, CN, halo, OH, NO2, nitrone, sulfonate, or (un)substituted alkoxy(carbonyl), alkenyl, alkyl, or (hetero)aryl; or 2 adjacent members of R1 to R5 = O- and together complex with C or a metal; provided that at least 1 of R1 to R5 = MeOCH2O or H(CH2CMe=CHCH2)n; n = 1-4; further provided that when R1 to R5 = MeOCH2O, R = Ph para-substituted by CN, NO2, nitroso, NHOH, NH2CO, alkyl ester, N-contg. heterocyclyl, etc.; R6 = H or (un)substituted alkoxycarbonyl; or stereoisomers or pharmaceutically acceptable salts thereof] were prepd. as **cytoprotective** agents useful in pharmaceutical and cosmetic formulations. For example, coupling of (4-nitrobenzyl)triphenylphosphoniu m bromide with 3,4-bis(methoxymethoxy)benzaldehyde using LiOEt in EtOH (41%) followed by deetherification with concd. HCl in EtOH gave 4-[2-(4-nitrophenyl)vinyl]benzene-1,2-diol (81%). The latter was among

invention compds. that showed significant redn. in edema in assays assessing rat paw edema (10 to 70%, $p < 0.05$) and mouse ear inflammatory response to topical arachidonic acid (15 to 80%, $p < 0.05$). Results from the neuronal cell stress assay and the rat middle cerebral artery occlusion model of cerebral **ischemia** were also disclosed for selected invention compds. Thus, I are useful in the treatment of certain **ischemic** or inflammatory conditions, including but not limited to stroke, myocardial infarction, congestive heart failure, and skin disorders characterized by inflammation or oxidative damage.

L102 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 2002:927398 CAPLUS
DOCUMENT NUMBER: 138:19518
TITLE: Sponge-derived terpenoids and their synthetic derivs. uses in treatment of lipoxygenase-mediated inflammatory conditions
INVENTOR(S): Crews, Phillip; Carroll, Jennifer; **Miller, Guy**; Bobzin, Steve; **Brown, Lesley**; Holman, Theodore
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096870	A2	20021205	WO 2002-US17171	20020531
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003065025	A1	20030403	US 2002-159772	20020531

PRIORITY APPLN. INFO.: US 2001-295258P P 20010531
OTHER SOURCE(S): MARPAT 138:19518
AB Compds. that are effective lipoxygenase inhibitors, and methods and pharmaceutical compns. for inhibiting lipoxygenases and for treatment of lipoxygenase-mediated conditions in humans and other subjects. The compds., methods and pharmaceutical compns. utilize subersic terpenoids, jaspic terpenoids, igernellic terpenoids, hippospongic terpenoids, halicondric terpenoids, dictyodendric terpenoids, and/or heteronemic terpenoids, and synthetic derivs. or analogs thereof. Exemplary compds. include (-)-subersic acid, (+)-subersin, jaspaquinol, (-)-jaspic acid, igernellin, halisufate 7, and hipposulfate C and D, and derivs. thereof.

L102 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 3
ACCESSION NUMBER: 2002:465811 CAPLUS
DOCUMENT NUMBER: 137:28330
TITLE: Compositions and methods for the treatment of tissue **ischemia**
INVENTOR(S): **Miller, Guy Michael; Brown, Lesley A.**; Del Balzo, Ughetta; Flaim, Stephen; Boddupalli, Sekhar; Wang, Bing
PATENT ASSIGNEE(S): Galileo Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 130 pp.

Searched by Barb O'Bryen, STIC 308-4291

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002047680	A2	20020620	WO 2001-US50984	20011214
WO 2002047680	A3	20030327		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002039748	A5	20020624	AU 2002-39748	20011214
US 2002132845	A1	20020919	US 2001-17717	20011214
US 2002143049	A1	20021003	US 2001-20450	20011214

PRIORITY APPLN. INFO.:
US 2000-256269P P 20001215
US 2001-296580P P 20010606
US 2001-296581P P 20010606
US 2001-343575P P 20011019
WO 2001-US50984 W 20011214

AB The present invention provides compns. and methods for the treatment of tissue **ischemia**, and in particular, cerebral **ischemia**. In particular, the present invention provides gamma-, beta-, or delta-tocopherol enriched tocopherol compns. and gamma-, beta, or delta-tocopherol metabolite enriched compns. and/or flavonoid enriched and/or a flavonoid deriv. enriched compns. and methods for their use in preventing or treating a tissue **ischemic** condition or a cerebral **ischemic** condition. The present invention also provides pharmaceutical compns. comprising gamma-, beta-, or delta-tocopherol enriched tocopherol compn., a gamma-, beta-, or delta-tocopherol metabolite enriched compns. or flavonoid enriched compns. or flavonoid deriv. enriched compns.

L102 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 4
ACCESSION NUMBER: 2002:570708 CAPLUS
DOCUMENT NUMBER: 137:119700
TITLE: Formulations of tocopherols and methods of making and using them
INVENTOR(S): **Miller, Guy; Brown, Lesley A.**
PATENT ASSIGNEE(S): Galileo Laboratories, Inc., USA
SOURCE: U.S., 28 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6426362	B1	20020730	US 2000-684588	20001006
US 2003022818	A1	20030130	US 2002-188587	20020702

PRIORITY APPLN. INFO.:
US 1999-158234P P 19991008
US 2000-684588 A1 20001006

AB Non-naturally-occurring compns. for use in amelioration of disruption of energy metab. secondary to stress are described. The compns. comprise a

tocopherol and/or a deriv. thereof, and a synergist, and are particularly suited for use as nutritional supplements. Synergists include, but are not limited to, flavonoids and lactoferrin and/or derivs. thereof. Compns. comprising an optimized formulation comprising a tocopherol and an addnl. compd. such as daidzein or biochanin A are also described. Methods of making these compns. and methods of ameliorating injury(ies) or disruption of energy metab. secondary to stress, comprising administering such compns., are also disclosed. Various concns. of tocopherols and flavonoids were tested in vitro for the combined ability to ameliorate disruption of energy metab. secondary to stress. For example, diosmin (3.3-100 .mu.M) was not protective by itself, but was synergistic in that range with 10 .mu.g/mL (.+-.)-.alpha.-tocopherol, a concn. at which (.+-.)-.alpha.-tocopherol was only slightly (about 15%) protective by itself. The combination of 100 .mu.M diosmin and 100 .mu.g/mL (.+-.)-.alpha.-tocopherol greatly reduced cell death, providing about 70% protection against stress-induced cell death, indicating synergism between these components. A combinations of 100 .mu.M diosmin and 11 .mu.g/mL (.+-.)-.alpha.-tocopherol was also synergistic.

REFERENCE COUNT: 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L102 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:169981 CAPLUS
DOCUMENT NUMBER: 138:180774
TITLE: Compositions of flavonoids and synergists for use as **cytoprotectants** and methods of making and using them
INVENTOR(S): **Brown, Lesley A.**; **Miller, Guy**
PATENT ASSIGNEE(S): Galileo Laboratories, Inc., USA
SOURCE: U.S., 28 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6528042	B1	20030304	US 2000-684607	20001006

PRIORITY APPLN. INFO.: US 1999-159003P P 19991008

AB Non-naturally-occurring compns. for use in amelioration of disruption of energy metab. secondary to stress are described. These compns. comprise a flavonoid or deriv. thereof and a synergist. Synergists include, but are not limited to, amino acids, carbohydrates, carnitines, flavonoids, nucleosides, and tocopherols and/or derivs. thereof. Methods of making these compns. and methods of ameliorating disruption of energy metab. secondary to stress, comprising administering such synergistic compns., are also disclosed.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L102 ANSWER 13 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002442933 EMBASE
TITLE: Attentional demands for static postural control after stroke.
AUTHOR: **Brown L.A.**; Sleik R.J.; Winder T.R.
CORPORATE SOURCE: Dr. L.A. Brown, Balance Research Laboratory, Department of Kinesiology, University of Lethbridge, 4401 University Dr, Lethbridge, Alb TIK 3M4, Canada. l.brown@uleth.ca
SOURCE: Archives of Physical Medicine and Rehabilitation, (1 Dec 2002) 83/12 (1732-1735).
Refs: 25
ISSN: 0003-9993 CODEN: APMHAI

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
019 Rehabilitation and Physical Medicine
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objective: To assess the attentional demands associated with postural control among people who have had a stroke. Design: Nonrandomized matched case-control study. Setting: University research laboratory in Canada. Participants: Six individuals who had suffered a left or right cerebral ischemic attack in the past year and a sample of 6 age-and gender-matched controls. Participants in the stroke group had a mean age of 64.17.+-.13.14 years; control participants had a mean age of 64.00.+-.13.91 years. Mean National Institute of Health Stroke Scale scores for these patients were 7.67.+-.4.92 at the time of stroke and 1.66.+-.1.36 at the time of testing. None of the patients were taking medications that would alter cognitive status or balance abilities. Intervention: Participants performed a verbal reaction-time test while engaged in 3 postural tasks (sitting, standing, standing with feet together). Main Outcome Measure: Reaction time: latency between visual stimulus and verbal response. Results: Reaction times in the stroke group differed significantly in all conditions from the controls (410.+-.72ms vs 320.+-.54ms, P<.01). A significant interaction was found between group and postural task (P=.05), with reaction-time scores showing a progressive increase in postural task difficulty among participants who had suffered a stroke. Post hoc comparisons revealed that sitting reaction-time scores were significantly slower than reaction-time scores for feet together standing (P=.008) among participants in the stroke group. Conclusion: Individuals who have suffered a stroke showed increased attentional demands for tasks of static postural control compared with healthy, age-matched participants. .COPYRGT. 2002 by the American Congress of Rehabilitation Medicine and the American Academy of Physical Medicine and Rehabilitation.

L102 ANSWER 14 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001327389 EMBASE
TITLE: Mr imaging in comatose survivors of cardiac resuscitation.
AUTHOR: Wijdicks E.F.M.; Campeau N.G.; **Miller G.M.**
CORPORATE SOURCE: Dr. E.F.M. Wijdicks, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, United States
SOURCE: American Journal of Neuroradiology, (2001) 22/8 (1561-1565).
Refs: 13
ISSN: 0195-6108 CODEN: AAJNDL
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 008 Neurology and Neurosurgery
014 Radiology
024 Anesthesiology
027 Biophysics, Bioengineering and Medical Instrumentation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB BACKGROUND AND PURPOSE: The prognosis of comatose survivors is determined by clinical examination. Early laboratory indicators of poor prognosis (such as evoked potentials) have low sensitivity. The role of MR imaging as a confirmatory study was investigated. METHODS: We studied fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted (DW) imaging in 10 patients comatose after cardiac arrest. RESULTS: None of the 10 comatose patients had myoclonus status epilepticus or fixed, dilated pupils on neurologic examination, and none had abnormal somatosensory-evoked potentials. Eight patients showed diffuse signal abnormalities, predominantly in the cerebellum (n = 5), the thalamus (n =

8), the frontal and parietal cortices (n = 8), and the hippocampus (n = 9). One patient showed normal MR imaging results, and one patient had abnormalities in the thalamus and cerebellum and minimal abnormality on DW images; both later awakened. None of the patients with abnormal cortical structures on FLAIR MR images recovered beyond a severely disabled state. CONCLUSION: MR imaging in comatose survivors may parallel the pathologic findings in severe anoxic-ischemic injury, and extensive abnormalities may indicate little to no prospects for recovery. If confirmed, MR imaging may have a role as a prognosticating test in anoxicischemic coma.

L102 ANSWER 15 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999102927 EMBASE
TITLE: Structural evidence of injury or malformation in the brains of children with congenital heart disease.
AUTHOR: **Miller G.**; Vogel H.
CORPORATE SOURCE: Dr. G. Miller, Pediatric Neurology Section, Texas Children's Hospital, MC3-3311, 6621 Fannin St, Houston, TX 77030, United States
SOURCE: Seminars in Pediatric Neurology, (1999) 6/1 (20-26). Refs: 47
ISSN: 1071-9091 CODEN: SPNEFD
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
008 Neurology and Neurosurgery
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Neurological and developmental deficits are common in children with congenital heart disease (CHD). These are due to multiple factors that include the etiology of the CHD, the effects of abnormal cardiovascular function, and the possible sequelae of open heart surgery. CHD is frequently part of a multiple malformation syndrome that includes the brain. The causes of these syndromes include known or putative genetic defects. Abnormal cardiovascular function may be associated with poor brain growth, embolic infarction, cerebrovascular thrombosis, and abscess formation. Perioperative neurological complications include diffuse hypoxic-ischemic injury (particularly in neonates who undergo more than 45 to 60 minutes of hypothermic circulatory arrest), cerebral macro- and micro-emboli, durai sinus thrombosis, and cerebral hemorrhage. Neuroimaging, especially magnetic resonance imaging, is a useful prognostic instrument, can easily display gross congenital and acquired lesions, and should be performed preoperatively in addition to genetic studies. In some instances poor brain function may not be predicted unless slow head growth or microcephaly is present and thorough preoperative neurodevelopmental evaluation is encouraged.

L102 ANSWER 16 OF 16 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2003-278496 [27] WPIDS
DOC. NO. CPI: C2003-072827
TITLE: Use of non-alpha tocopherols and their metabolites for reducing levels of inflammatory markers and thus ameliorating the symptoms of inflammation.
DERWENT CLASS: B02 C02
INVENTOR(S): BEINLICH, P; BODDUPALLI, S; **BROWN, L A**; DREON, D M; FLAIM, S; **MILLER, G**; PHINNEY, S D; **BROWN, L**
PATENT ASSIGNEE(S): (BEIN-I) BEINLICH P; (BODD-I) BODDUPALLI S; (BROW-I) BROWN L A; (DREO-I) DREON D M; (FLAI-I) FLAIM S; (MILL-I) MILLER G; (PHIN-I) PHINNEY S D; (GALI-N) GALILEO LAB INC
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003015494	A2	20030227	(200327)*	EN	32
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					
US 2003100603	A1	20030529	(200337)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003015494	A2	WO 2002-US26920	20020821
US 2003100603	A1 Provisional	US 2001-314223P	20010821
	Provisional	US 2001-314256P	20010821
	Provisional	US 2001-314257P	20010821
		US 2002-227094	20020821

PRIORITY APPLN. INFO: US 2001-314257P 20010821; US 2001-314223P 20010821; US 2001-314256P 20010821; US 2002-227094 20020821

AB WO2003015494 A UPAB: 20030429

NOVELTY - Reducing the level of an inflammatory marker, especially C-reactive protein (CRP), in an individual subject to an inflammatory condition comprises administering a non-alpha tocopherol or non-alpha tocopherol metabolite enriched tocopherol composition.

USE - The method is used to reduce one or more biochemical markers of inflammation, thereby reducing or ameliorating the symptoms of inflammation associated with disease and disorders including cardiovascular diseases or disorders (including atrial fibrillation, unstable angina, coronary artery disease, peripheral artery disease and cardiac allograft vaculopathy), mastitis, pre-eclampsia, inflammatory bowel conditions, stroke, tissue infarction, lumbosciatica, estrogen/progestin hormone replacement therapy, infection (bacterial, viral or protozoal), bacterial meningitis, trauma, surgery, biomaterial implants, smoking, obesity, neurodegenerative diseases (e.g. Alzheimer's), infectious disease (sic) (e.g. myocarditis, cardiomyopathy, acute endocarditis or pericarditis), atherosclerosis, systemic inflammatory response syndrome/sepsis, adult respiratory distress syndrome, asthma, rheumatoid arthritis, osteoarthritis, systemic lupus erythematosus, airway hyper-responsiveness, bronchial hyper-reactivity, chronic obstructive pulmonary disease, congestive heart failure, inflammatory complication of diabetes type I and II, metabolic syndrome, end-stage renal disease, pre-menstrual syndrome or muscle fatigue or inflammation, multiple organ dysfunction syndrome, aging, acute allergic reactions, gingivitis and dermal conditions.

ADVANTAGE - Reduction of inflammatory markers improves prognosis and reduces mortality related to inflammatory diseases.

Dwg.0/0

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=> fil uspatf; d que l101
FILE 'USPATFULL' ENTERED AT 13:06:42 ON 17 JUN 2003
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 17 Jun 2003 (20030617/PD)
FILE LAST UPDATED: 17 Jun 2003 (20030617/ED)
HIGHEST GRANTED PATENT NUMBER: US6581208
HIGHEST APPLICATION PUBLICATION NUMBER: US2003110547
CA INDEXING IS CURRENT THROUGH 17 Jun 2003 (20030617/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 17 Jun 2003 (20030617/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2003

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>>>  /PK, etc.                                                         <<<

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>>>  classifications, or claims, that may potentially change from     <<<
>>>  the earliest to the latest publication.                           <<<

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substance identification.


L9              1 SEA FILE=REGISTRY ABB=ON  178167-88-9/RN
L101            6 SEA FILE=USPATFULL ABB=ON  L9          chroman deriv.


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=> d que l27; d que l28; d que l30

L9            1 SEA FILE=REGISTRY ABB=ON  178167-88-9/RN
L13          19 SEA FILE=CAPLUS ABB=ON  L9
L19        2758 SEA FILE=CAPLUS ABB=ON  ANTI-ISCHEMIC AGENTS/CT
L20        5680 SEA FILE=CAPLUS ABB=ON  ISCHEMIA/CT
L21        9061 SEA FILE=CAPLUS ABB=ON  NERVE#/CT(L)(DAMAG? OR DEATH)
L22        1197 SEA FILE=CAPLUS ABB=ON  CEREBRAL(L) INFARCT?/OBI
L23        8507 SEA FILE=CAPLUS ABB=ON  STROKE/OBI
L24        1984 SEA FILE=CAPLUS ABB=ON  CEREBRAL(L)EDEMA?
L25        1496 SEA FILE=CAPLUS ABB=ON  MENTAL DISORDER/CT(L)COGNITIVE
L26        1879 SEA FILE=CAPLUS ABB=ON  COGNITI?(L)(DYSFUNCTION? OR DISORDER?)/
                OBI
L27           1 SEA FILE=CAPLUS ABB=ON  L13 AND (L19 OR L20 OR L21 OR L22 OR
                L23 OR L24 OR L25 OR L26)



L10           1 SEA FILE=REGISTRY ABB=ON  .BETA.-TOCOPHEROL/CN
L11           1 SEA FILE=REGISTRY ABB=ON  .DELTA.-TOCOPHEROL/CN
L12           1 SEA FILE=REGISTRY ABB=ON  .GAMMA.-TOCOPHEROL/CN
L14        1189 SEA FILE=CAPLUS ABB=ON  L10
L15        1525 SEA FILE=CAPLUS ABB=ON  L11
L16        2299 SEA FILE=CAPLUS ABB=ON  L12
L19        2758 SEA FILE=CAPLUS ABB=ON  ANTI-ISCHEMIC AGENTS/CT
L20        5680 SEA FILE=CAPLUS ABB=ON  ISCHEMIA/CT
L21        9061 SEA FILE=CAPLUS ABB=ON  NERVE#/CT(L)(DAMAG? OR DEATH)
L22        1197 SEA FILE=CAPLUS ABB=ON  CEREBRAL(L) INFARCT?/OBI
L23        8507 SEA FILE=CAPLUS ABB=ON  STROKE/OBI
L24        1984 SEA FILE=CAPLUS ABB=ON  CEREBRAL(L)EDEMA?
L25        1496 SEA FILE=CAPLUS ABB=ON  MENTAL DISORDER/CT(L)COGNITIVE
L26        1879 SEA FILE=CAPLUS ABB=ON  COGNITI?(L)(DYSFUNCTION? OR DISORDER?)/
                OBI
L28           5 SEA FILE=CAPLUS ABB=ON  (L14 OR L15 OR L16) AND (L19 OR L20 OR
                L21 OR L22 OR L23 OR L24 OR L25 OR L26)



L9            1 SEA FILE=REGISTRY ABB=ON  178167-88-9/RN
L10           1 SEA FILE=REGISTRY ABB=ON  .BETA.-TOCOPHEROL/CN
L11           1 SEA FILE=REGISTRY ABB=ON  .DELTA.-TOCOPHEROL/CN
L12           1 SEA FILE=REGISTRY ABB=ON  .GAMMA.-TOCOPHEROL/CN
L13          19 SEA FILE=CAPLUS ABB=ON  L9
L14        1189 SEA FILE=CAPLUS ABB=ON  L10
L15        1525 SEA FILE=CAPLUS ABB=ON  L11
L16        2299 SEA FILE=CAPLUS ABB=ON  L12
L29       11670 SEA FILE=CAPLUS ABB=ON  NEURON?(2A)(DEATH OR DAMAG?)
L30           0 SEA FILE=CAPLUS ABB=ON  L29 AND (L13 OR L14 OR L15 OR L16)

=> s (127 or 128) not 15
L104          3 (L27 OR L28) NOT L5
=> fil medl
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previously omitted cc/ inventors

FILE 'MEDLINE' ENTERED AT 13:06:44 ON 17 JUN 2003

FILE LAST UPDATED: 14 JUN 2003 (20030614/UP). FILE COVERS 1958 TO DATE.

Searched by Barb O'Bryen, STIC 308-4291

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> d que l42; d que l52

L9            1 SEA FILE=REGISTRY ABB=ON  178167-88-9/RN
L10           1 SEA FILE=REGISTRY ABB=ON  .BETA.-TOCOPHEROL/CN
L11           1 SEA FILE=REGISTRY ABB=ON  .DELTA.-TOCOPHEROL/CN
L12           1 SEA FILE=REGISTRY ABB=ON  .GAMMA.-TOCOPHEROL/CN
L42           0 SEA FILE=MEDLINE ABB=ON  (L9 OR L10 OR L11 OR L12)


L34         592 SEA FILE=MEDLINE ABB=ON  TOCOPHEROLS+NT/CT
L35        3706 SEA FILE=MEDLINE ABB=ON  CHROMANS+NT/CT
L37         183 SEA FILE=MEDLINE ABB=ON  SPINAL CORD ISCHEMIA+NT/CT
L52           0 SEA FILE=MEDLINE ABB=ON  (L34 OR L35) AND L37


=> d que l57;d que l58;d que l63; d que l71

L34         592 SEA FILE=MEDLINE ABB=ON  TOCOPHEROLS+NT/CT
L36       35432 SEA FILE=MEDLINE ABB=ON  HYPOXIA-ISCHEMIA, BRAIN+NT/CT
L37         183 SEA FILE=MEDLINE ABB=ON  SPINAL CORD ISCHEMIA+NT/CT
L38      242997 SEA FILE=MEDLINE ABB=ON  NEURONS+NT/CT
L39      109454 SEA FILE=MEDLINE ABB=ON  CELL DEATH+NT/CT
L40        8017 SEA FILE=MEDLINE ABB=ON  BRAIN EDEMA/CT
L41       15395 SEA FILE=MEDLINE ABB=ON  COGNITION DISORDERS+NT/CT
L43       13854 SEA FILE=MEDLINE ABB=ON  NERVE DEGENERATION+NT/CT
L56         114 SEA FILE=MEDLINE ABB=ON  L34 NOT ALPHA-TOCOPHEROL/CT
L57           1 SEA FILE=MEDLINE ABB=ON  L56 AND ((L36 OR L37) OR (L38 AND
                L39) OR (L40 OR L41) OR L43)


L34         592 SEA FILE=MEDLINE ABB=ON  TOCOPHEROLS+NT/CT
L36       35432 SEA FILE=MEDLINE ABB=ON  HYPOXIA-ISCHEMIA, BRAIN+NT/CT
L37         183 SEA FILE=MEDLINE ABB=ON  SPINAL CORD ISCHEMIA+NT/CT
L38      242997 SEA FILE=MEDLINE ABB=ON  NEURONS+NT/CT
L39      109454 SEA FILE=MEDLINE ABB=ON  CELL DEATH+NT/CT
L40        8017 SEA FILE=MEDLINE ABB=ON  BRAIN EDEMA/CT
L41       15395 SEA FILE=MEDLINE ABB=ON  COGNITION DISORDERS+NT/CT
L43       13854 SEA FILE=MEDLINE ABB=ON  NERVE DEGENERATION+NT/CT
L58           1 SEA FILE=MEDLINE ABB=ON  L34 AND (BETA OR DELTA OR GAMMA) AND
                ((L36 OR L37) OR (L38 AND L39) OR (L40 OR L41) OR L43)


L35        3706 SEA FILE=MEDLINE ABB=ON  CHROMANS+NT/CT
L36       35432 SEA FILE=MEDLINE ABB=ON  HYPOXIA-ISCHEMIA, BRAIN+NT/CT
L37         183 SEA FILE=MEDLINE ABB=ON  SPINAL CORD ISCHEMIA+NT/CT
L38      242997 SEA FILE=MEDLINE ABB=ON  NEURONS+NT/CT
L39      109454 SEA FILE=MEDLINE ABB=ON  CELL DEATH+NT/CT
L40        8017 SEA FILE=MEDLINE ABB=ON  BRAIN EDEMA/CT
L41       15395 SEA FILE=MEDLINE ABB=ON  COGNITION DISORDERS+NT/CT
L43       13854 SEA FILE=MEDLINE ABB=ON  NERVE DEGENERATION+NT/CT
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L63           3 SEA FILE=MEDLINE ABB=ON  L35 AND (L36 OR L37) AND ((L38 AND
                L39) OR L40 OR L41 OR L43)



L34         592 SEA FILE=MEDLINE ABB=ON  TOCOPHEROLS+NT/CT
L56         114 SEA FILE=MEDLINE ABB=ON  L34 NOT ALPHA-TOCOPHEROL/CT
L68        5864 SEA FILE=MEDLINE ABB=ON  NEUROPROTECTIVE AGENTS/CT
L70         270 SEA FILE=MEDLINE ABB=ON  L56 OR (L34 AND (BETA OR DELTA OR
                GAMMA))
L71           1 SEA FILE=MEDLINE ABB=ON  L70 AND L68


=> s (157 or 158 or 163 or 171) not 167

L105          5 (L57 OR L58 OR L63 OR L71) NOT L67

=> fil embase; d que 186

FILE 'EMBASE' ENTERED AT 13:06:47 ON 17 JUN 2003
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 FILE COVERS 1974 TO 12 Jun 2003 (20030612/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L9            1 SEA FILE=REGISTRY ABB=ON  178167-88-9/RN
L10           1 SEA FILE=REGISTRY ABB=ON  .BETA.-TOCOPHEROL/CN
L11           1 SEA FILE=REGISTRY ABB=ON  .DELTA.-TOCOPHEROL/CN
L12           1 SEA FILE=REGISTRY ABB=ON  .GAMMA.-TOCOPHEROL/CN
L72         546 SEA FILE=EMBASE ABB=ON  BETA TOCOPHEROL/CT OR DELTA TOCOPHEROL/
                CT OR GAMMA TOCOPHEROL/CT
L73         546 SEA FILE=EMBASE ABB=ON  (L9 OR L10 OR L11 OR L12)
L77       27750 SEA FILE=EMBASE ABB=ON  BRAIN ISCHEMIA+NT/CT
L78       15428 SEA FILE=EMBASE ABB=ON  BRAIN INFARCTION+NT/CT OR BRAIN
                INFARCTION SIZE/CT
L79        7190 SEA FILE=EMBASE ABB=ON  BRAIN EDEMA/CT
L80       14708 SEA FILE=EMBASE ABB=ON  COGNITIVE DEFECT/CT
L81        3563 SEA FILE=EMBASE ABB=ON  NERVE CELL DEGENERATION/CT
L82        4464 SEA FILE=EMBASE ABB=ON  NERVE CELL NECROSIS/CT
L83        8533 SEA FILE=EMBASE ABB=ON  NEUROPROTECTIVE AGENT/CT OR NEUROPROTEC
                TION/CT
L86           3 SEA FILE=EMBASE ABB=ON  (L72 OR L73) AND (L77 OR L78 OR L79 OR
                L80 OR L81 OR L82 OR L83)


=> s l86 not 184

L106          3 L86 NOT L84

=> fil wpids; d que l100

FILE 'WPIDS' ENTERED AT 13:06:48 ON 17 JUN 2003
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FILE LAST UPDATED:          16 JUN 2003      <20030616/UP>
MOST RECENT DERWENT UPDATE:     200338        <200338/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
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>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

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    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<


L90          314 SEA FILE=WPIDS ABB=ON  (GAMMA OR BETA OR DELTA OR NONALPHA OR
                 NON ALPHA)(A)TOCOPHEROL#
L91          282 SEA FILE=WPIDS ABB=ON  CHROMAN DERIVATIVE#
L92         2225 SEA FILE=WPIDS ABB=ON  (NERVE OR NEURON?)(3A)(DAMAG? OR INJUR?
                 OR DEATH OR NECROSIS OR APOPTOSIS)
L93         3332 SEA FILE=WPIDS ABB=ON  (BRAIN OR CEREBRAL)(2A)(ISCHEM? OR
                 ISCHAEM?)
L94         1950 SEA FILE=WPIDS ABB=ON  (CEREBRAL OR BRAIN)(2A)INFARCT?
L95        64833 SEA FILE=WPIDS ABB=ON  STROKE OR (ISCHEM? OR ISCHAEM?)(W)ACCIDE
                 NT#
L96          710 SEA FILE=WPIDS ABB=ON  (BRAIN OR CEREBRAL)(3A)(EDEMA? OR
                 CEDEMA?)
L97         1404 SEA FILE=WPIDS ABB=ON  COGNITI?(2A)(DYSFUNCTION? OR DISORDER?
                 OR DEFECT?)
L98        10334 SEA FILE=WPIDS ABB=ON  NEUROPROTECT? OR NEURO PROTECT?
L100          10 SEA FILE=WPIDS ABB=ON  (L90 OR L91) AND L93 AND (L92 OR (L94
                 OR L95 OR L96 OR L97 OR L98))


=> s l100 not l89

L107           9 L100 NOT L89
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previously printed

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=> dup rem l105,l104,l106,l107,l101
FILE 'MEDLINE' ENTERED AT 13:07:39 ON 17 JUN 2003

FILE 'CAPLUS' ENTERED AT 13:07:39 ON 17 JUN 2003
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FILE 'USPATFULL' ENTERED AT 13:07:39 ON 17 JUN 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
PROCESSING COMPLETED FOR L105
PROCESSING COMPLETED FOR L104
PROCESSING COMPLETED FOR L106
PROCESSING COMPLETED FOR L107
PROCESSING COMPLETED FOR L101
L108          25 DUP REM L105 L104 L106 L107 L101 (1 DUPLICATE REMOVED)
                 ANSWERS '1-5' FROM FILE MEDLINE
                 ANSWERS '6-8' FROM FILE CAPLUS
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ANSWERS '9-11' FROM FILE EMBASE
ANSWERS '12-20' FROM FILE WPIDS
ANSWERS '21-25' FROM FILE USPATFULL

=> d ibib ab hitrn 1-25; fil hom

L108 ANSWER 1 OF 25 MEDLINE
ACCESSION NUMBER: 2002694975 MEDLINE
DOCUMENT NUMBER: 22345634 PubMed ID: 12457865
TITLE: Long term dietary supplementation with zeaxanthin reduces photoreceptor death in light-damaged Japanese quail.
AUTHOR: Thomson Lauren R; Toyoda Yoko; Delori Francois C; Garnett Kevin M; Wong Z Y; Nichols Cathleen R; Cheng Kimberly M; Craft Neal E; Kathleen Dorey C
CORPORATE SOURCE: Schepens Eye Research Institute and Department of Ophthalmology, Harvard Medical School, Boston, MA, USA.
SOURCE: EXPERIMENTAL EYE RESEARCH, (2002 Nov) 75 (5) 529-42. Journal code: 0370707. ISSN: 0014-4835.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021214
Last Updated on STN: 20021218
Entered Medline: 20021213

AB The purpose of these studies was to evaluate the effects of light damage on Japanese quail whose retinal carotenoids had been experimentally manipulated through altered diets. The birds were raised 6 months on a commercial turkey diet (T), on a custom carotenoid-deficient diet (C-) containing 90% less carotenoid than the T diet, or on Z+ diet [the C- diet supplemented with natural zeaxanthin (35mgkg(-1) food)]. Equal numbers of males and females on each diet were exposed to nine intervals (1hr on, 2hr off) of 3200lux cool white light, then placed in the dark for 14hr before tissue collection. One retina was immediately frozen for HPLC analysis; the other eye was immediately fixed and processed for microscopy. There were no significant differences in the retinal carotenoid concentrations in hatch-mates that were and were not exposed to light. Supplementation resulted in three- to four-fold increases in retinal zeaxanthin and no change in retinal lutein or alpha-tocopherol, but the C- diet did not reduce the retinal carotenoid concentration in C- birds below that in T birds. The light-exposed retinas had significant numbers of apoptotic photoreceptors and photoreceptor ghosts. The number of ghosts was negatively correlated with the number of dying photoreceptors ($P<0.05$), and with retinal concentrations of zeaxanthin, alpha-tocopherol or **gamma**-tocopherol ($P<0.04$, 0.02, 0.04, respectively), but not with lutein. The number of dying photoreceptors was positively correlated with alpha-tocopherol and the sum alpha-tocopherol plus zeaxanthin ($P<0.1$; P0.04). Photoreceptor death was semi-quantitatively scored, assuming that ghosts were formed by removal of apoptotic photoreceptors with nuclear condensation. Stepwise regression produced a good model ($r(2)=0.67$; $P<0.0001$) for predicting death scores from retinal concentrations of zeaxanthin (Standard Coefficient=-0.76) and lutein (Standard Coefficients=+0.43). Absence of lutein in gender-specific analyses suggests lutein served as surrogate marker for gender. Combined analysis of the C- and T birds also demonstrated that dying photoreceptors were negatively correlated with retinal zeaxanthin. These data confirm our previous report that retinal carotenoids prevent photoreceptor cell death, and provide the first direct evidence that retinal zeaxanthin protects photoreceptors from light-induced death.

L108 ANSWER 2 OF 25 MEDLINE
ACCESSION NUMBER: 2001640907 MEDLINE

DOCUMENT NUMBER: 21550120 PubMed ID: 11692230
TITLE: Neuroprotection afforded by some hindered phenols and alpha-tocopherol in guinea-pig detrusor strips subjected to anoxia-glucopenia and reperfusion-like conditions.
AUTHOR: Pessina F; Kalfin R; Esposito L; Fusi F; Valoti M; Ponticelli F; Sgaragli G
CORPORATE SOURCE: Istituto di Scienze Farmacologiche, Universita di Siena, Via E.S. Piccolomini 170, 53100 Siena, Italy.
SOURCE: NAUNYN-SCHMIEDEBERGS ARCHIVES OF PHARMACOLOGY, (2001 Nov) 364 (5) 462-71.
Journal code: 0326264. ISSN: 0028-1298.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011107
Last Updated on STN: 20020125
Entered Medline: 20020115

AB 2-t-butyl-4-methoxyphenol (BHA), 3,5-di-t-butyl-hydroxyanisole (DTBHA), 2,6-diisopropylphenol (propofol), alpha-tocopherol (alpha-TOC) and two newly synthesised analogues of BHA, namely 1-O-(4-hydroxy-3-t-butyl)phenyl-2,3,4,6-tetra-O-acetyl-**beta**-D-glucopyranose (**beta**-TAG) and 1-O-(4-hydroxy-3-t-butyl)phenyl-**beta**-D-glucopyranose (**beta**-GLU), were tested for their capability to protect the intrinsic nerves of guinea-pig urinary bladder from damage due to anoxia-glucopenia and re-exposure to glucose and O2. Guinea-pig detrusor strips were mounted for tension recording in small organ baths, superfused with warmed Krebs solution and the nerves stimulated electrically either under control or ischaemia-like (anoxia-glucopenia) and reperfusion-like conditions (normal medium re-superfusion). The Ca2+ antagonist activity of the compounds was assessed by their effect on the contraction of detrusor strips induced by 60 mM K+ Krebs solution in the presence of either 0.5 mM or 5 mM Ca2+. The antioxidant activity was illustrated by the ability of the compounds to scavenge peroxyl radicals generated by linoleic acid oxidation. All the compounds, except **beta**-GLU and alpha-TOC, inhibited in a concentration-dependent manner K+-induced contractions of detrusor muscles, the inhibition being inversely related to the Ca2+ concentration of the perfusion solution; moreover, they exhibited a marked antiperoxidant activity with pIC50 values decreasing in the order: DTBHA > alpha-TOC > BHA > **beta**-TAG > propofol > **beta**-GLU. alpha-TOC, BHA, DTBHA and **beta**-TAG improved significantly the response of the strips to electrical field stimulation either during the anoxia-glucopenia phase or thereafter when recovering during reperfusion, as compared to untreated tissues. The neuroprotection afforded by the phenol derivatives as well as by alpha-TOC was positively correlated to their antioxidant activity, but not to their Ca2+ antagonist activity.

L108 ANSWER 3 OF 25 MEDLINE
ACCESSION NUMBER: 1999196504 MEDLINE
DOCUMENT NUMBER: 99196504 PubMed ID: 10098868
TITLE: Mediation by membrane protein kinase C of zinc-induced oxidative neuronal injury in mouse cortical cultures.
AUTHOR: Noh K M; Kim Y H; Koh J Y
CORPORATE SOURCE: National Creative Research Initiative Center for the Study of CNS Zinc and Department of Neurology, Ulsan University School of Medicine, Seoul, Korea.
SOURCE: JOURNAL OF NEUROCHEMISTRY, (1999 Apr) 72 (4) 1609-16.
Journal code: 2985190R. ISSN: 0022-3042.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990426
Last Updated on STN: 20021219
Entered Medline: 19990413

AB Transsynaptic movement of endogenous zinc may play a key role in selective neuronal death after brain ischemia and prolonged seizures. As to the mechanism, we have reported recently that zinc-induced neuronal death occurs mainly by oxidative stress in cortical cultures. Here we present evidence supporting the idea that activation of membrane protein kinase C (PKC) in neurons is likely to play a key role in zinc-induced oxidative neuronal injury. Exposure of cortical cultures to 300 microM zinc for 15 min induced increases in the activity, without changing the amount, of membrane PKC to two- to threefold of control values, followed by neuronal death over the next day. Addition of a zinc chelator, Ca-EDTA, or PKC inhibitors with zinc completely abolished the zinc-induced increase in the membrane PKC activity. Indicating the participation of PKC in zinc-induced oxidative stress and neuronal death, the selective PKC inhibitor GF109203X attenuated both. Furthermore, as in zinc-induced neuronal death, activation of PKC with phorbol esters induced free radical generation and neuronal death, which were blocked by GF109203X or an antioxidant, Trolox. The present results support the idea that zinc influx activates PKC in the membrane, which contributes to free radical generation and neuronal death. As an increasing body of evidence suggests that zinc neurotoxicity is an important mechanism of pathological neuronal death, timely prevention of PKC activation after acute brain insult may prove useful in ameliorating this type of neuronal death.

L108 ANSWER 4 OF 25 MEDLINE
ACCESSION NUMBER: 1999075394 MEDLINE
DOCUMENT NUMBER: 99075394 PubMed ID: 9860051
TITLE: Oral administration of (-)catechin protects against ischemia-reperfusion-induced neuronal death in the gerbil.
AUTHOR: Inanami O; Watanabe Y; Syuto B; Nakano M; Tsuji M; Kuwabara M
CORPORATE SOURCE: Department of Radiation Biology, Faculty of Veterinary Medicine, Hokkaido University, Sapporo, Japan.. inanami@vetmed.hokudai.ac.jp
SOURCE: FREE RADICAL RESEARCH, (1998 Oct) 29 (4) 359-65. Journal code: 9423872. ISSN: 1071-5762.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990311
Last Updated on STN: 20000303
Entered Medline: 19990223

AB The effect of ad libitum oral-administration of (-)catechin solution on ischemia-reperfusion-induced cell death of hippocampal CA1 in the gerbil was histologically examined. When (-)catechin solution instead of drinking water was orally administered ad libitum for 2 weeks, dose-dependent protection against neuronal death following by transient ischemia and reperfusion was observed. To evaluate the involvement of reduction of reactive-oxygen-species (ROIs) by the antioxidant activity of (-)catechin in this protection, the superoxide scavenging activity of the brain in catechin-treated gerbils was measured by ESR and spin-trapping using 5,5-dimethyl-1-pyrroline-N-oxide (DMPO). The superoxide scavenging activities of the brains obtained from catechin-treated gerbils were significantly higher than those of catechin-untreated animals. From these results, it was suggested that orally administered (-)catechin was absorbed, passed through the blood-brain barrier and that delayed neuronal death of hippocampal CA1 after ischemia-reperfusion was prevented due to

its antioxidant activities.

L108 ANSWER 5 OF 25 MEDLINE
ACCESSION NUMBER: 1998186662 MEDLINE
DOCUMENT NUMBER: 98186662 PubMed ID: 9518539
TITLE: Trolox and 6,7-dinitroquinoxaline-2,3-dione prevent necrosis but not apoptosis in cultured neurons subjected to oxygen deprivation.
AUTHOR: Copin J C; Li Y; Reola L; Chan P H
CORPORATE SOURCE: CNS Injury and Edema Research Center, Department of Neurological Surgery, University of California, San Francisco, CA 94143-0651, USA.
CONTRACT NUMBER: NS 14543 (NINDS)
NS 25372 (NINDS)
NS 36147 (NINDS)
+
SOURCE: BRAIN RESEARCH, (1998 Feb 16) 784 (1-2) 25-36.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980507
Last Updated on STN: 20000303
Entered Medline: 19980430

AB There is a growing body of evidence suggesting that apoptosis is involved in ischemic brain injury. Recent studies suggest that a rapid necrosis masked a more subtle apoptotic death in neurons subjected to oxygen deprivation in culture. To test this hypothesis, we treated cultured neurons with potential antinecrotic drugs during and after oxygen deprivation. The results show that 6, 7-dinitroquinoxaline-2,3-dione (DNQX) and 6-hydroxy-2,5,7, 8-tetramethylchroman-2-carboxylic acid (Trolox), which interfered with kainate receptor activation and lipid peroxidation respectively, prevented necrosis but allowed neurons to undergo apoptosis. Flow cytometric analysis of DNA degradation and hydrogen peroxide generation, as well as fluorescent microscopy of nuclear fragmentation revealed that apoptotic activity was higher in 6, 7-dinitroquinoxaline-2,3-dione-treated cells than in Trolox-treated cells. This difference in occurrence of apoptosis may be due to the difference in oxidative stress generated from these two different agents.

L108 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 2000:238052 CAPLUS
DOCUMENT NUMBER: 132:260686
TITLE: Use of .gamma.-tocopherol and its oxidative metabolite LLU-.alpha. in the treatment of natriuretic disease
INVENTOR(S): Wechter, William J.
PATENT ASSIGNEE(S): Loma Linda University Medical Center, USA
SOURCE: U.S., 21 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6048891	A	20000411	US 1998-215608	19981217
US 6242479	B1	20010605	US 1999-461645	19991214
WO 2000035444	A1	20000622	WO 1999-US30100	19991216
W: AU, CA, JP				

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
EP 1140065 A1 20011010 EP 1999-968905 19991216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2002532421 T2 20021002 JP 2000-587764 19991216
US 2001031782 A1 20011018 US 2001-814330 20010321
US 6410589 B2 20020625
US 2002165268 A1 20021107 US 2002-134140 20020426
US 6555575 B2 20030429
PRIORITY APPLN. INFO.: US 1998-215608 A1 19981217
US 1999-461645 A1 19991214
WO 1999-US30100 W 19991216
US 2001-814330 A1 20010321
OTHER SOURCE(S): MARPAT 132:260686
AB The invention is generally related to the discovery of the therapeutic benefit of administering .gamma.-tocopherol and .gamma.-tocopherol derivs. More specifically, the use of .gamma.-tocopherol and racemic LLU-.alpha., (S)-LLU-.alpha., or .gamma.-tocopherol derivs. as antioxidants and nitrogen oxide scavengers which treat and prevent high blood pressure, thromboembolic disease, cardiovascular disease, cancer, natriuretic disease, the formation of neuropathol. lesions, and a reduced immune system response are disclosed.
IT **178167-88-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(.gamma.-tocopherol and oxidative metabolite LLU-.alpha. in treatment of natriuretic disease)
IT **119-13-1**, .delta.-Tocopherol **148-03-8**, .beta.-Tocopherol **7616-22-0**, .gamma.-Tocopherol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma.-tocopherol and oxidative metabolite LLU-.alpha. in treatment of natriuretic disease)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L108 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:169475 CAPLUS
DOCUMENT NUMBER: 128:248580
TITLE: Association of NO synthase inhibitors with trappers of reactive oxygen species
INVENTOR(S): Chabrier De Lassauniere, Pierre-Etienne; Bigg, Denis
PATENT ASSIGNEE(S): Societe De Conseils De Recherches Et D'applications Scientifiques (S.C.R.A.S, Fr.; Chabrier De Lassauniere, Pierre-Etienne; Bigg, Denis
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9809653	A1	19980312	WO 1997-FR1567	19970905

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

FR 2753098	A1	19980313	FR 1996-10875	19960906	
FR 2753098	B1	19981127			
AU 9742111	A1	19980326	AU 1997-42111	19970905	
AU 734296	B2	20010607			
EP 939654	A1	19990908	EP 1997-940183	19970905	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
NZ 334597	A	20001027	NZ 1997-334597	19970905	
JP 2000517336	T2	20001226	JP 1998-512314	19970905	
RU 2174844	C2	20011020	RU 1999-106792	19970905	
US 6297281	B1	20011002	US 1999-254254	19990302	
NO 9901100	A	19990505	NO 1999-1100	19990305	

PRIORITY APPLN. INFO.: FR 1996-10875 A 19960906
WO 1997-FR1567 W 19970905

AB The invention concerns a pharmaceutical compn. contg., as active principle, at least one NO synthase-inhibiting substance and at least one reactive oxygen-trapping substance, optionally with a pharmaceutically acceptable support. The invention also concerns a product contg. at least one NO synthase-inhibiting substance and at least one reactive oxygen-trapping substance as combined product of these active principles in sep. form.

IT **119-13-1**, .delta.-Tocopherol **148-03-8**, .beta.-Tocopherol **7616-22-0**, .gamma.-Tocopherol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(assocn. of NO synthase inhibitors with trappers of reactive oxygen species)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L108 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:755384 CAPLUS
DOCUMENT NUMBER: 130:119508
TITLE: Plasma antioxidants and cognitive performance in middle-aged and older adults: Results of the Austrian **stroke** prevention study
AUTHOR(S): Schmidt, R.; Hayn, M.; Reinhart, B.; Roob, G.; Schmidt, H.; Schumacher, M.; Watzinger, N.; Launer, L. J.
CORPORATE SOURCE: Departments of Neurology, Karl -Franzens University Graz, Graz, Austria
SOURCE: Journal of the American Geriatrics Society (1998), 46(11), 1407-1410
CODEN: JAGSAF; ISSN: 0002-8614
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The assocn. between cognitive status and blood plasma concns. of various antioxidants in middle-aged and older individuals without neuropsychiatric disease was studied by evaluation of cross-sectional data from a cohort study. A total of 1769 subjects aged 50-75 yr, with no history or signs of neuropsychiatric disease was selected randomly from the community register. The score on the Mattis Dementia Rating Scale (MDRS) was dichotomized according to age-and education-specific lowest quartile cut-off points. Reversed-phase HPLC measurements of plasma concns. of lutein/zeaxanthin, cryptoxanthin, canthaxanthin, lycopene, .alpha.-carotene, .beta.-carotene, retinol, .gamma.-tocopherol, .alpha.-tocopherol, and ascorbate were measured. Individuals with MDRS results below the lowest quartile cut-off point had lower levels of

.beta.-carotene and .alpha.-tocopherol than their counterparts with test performance above this limit (0.44 .+-. .33 .mu.M vs. 0.51 .+-. .48 .mu.M, P < 0.001; and 29.50 .+-. 7.98 .mu.M vs. 30.93 .+-. 11.10 .mu.M, P < 0.001, resp.). Only .alpha.-tocopherol remained significantly assocd. with cognitive functioning when logistic regression anal. was used to adjust for possible confounders including age, sex, month of blood sampling, years of education, smoking, lipid status, and major risk factors for stroke (P = 0.019). Thus, these observations were compatible with the view that some dietary antioxidants may protect against cognitive impairment in older people.

IT **7616-22-0**, .gamma.-Tocopherol
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(plasma antioxidants and cognitive performance in middle-aged and older adults: results of the Austrian **stroke** prevention study)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L108 ANSWER 9 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003030610 EMBASE
TITLE: Vitamin E isoforms .alpha.-tocotrienol and .gamma.-tocopherol prevent cerebral infarction in mice.
AUTHOR: Mishima K.; Tanaka T.; Pu F.; Egashira N.; Iwasaki K.; Hidaka R.; Matsunaga K.; Takata J.; Karube Y.; Fujiwara M.
CORPORATE SOURCE: M. Fujiwara, Department of Neuropharmacology, Faculty of Pharmaceutical Sciences, Fukuoka University, Fukuoka 814-0180, Japan. mfuji@fukuoka-u.ac.jp
SOURCE: Neuroscience Letters, (30 Jan 2003) 337/1 (56-60).
Refs: 23
ISSN: 0304-3940 CODEN: NELED5
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB .alpha.-tocopherol and its derivatives have been shown to be effective in reducing cerebral ischemia-induced brain damage. However, the effects of other vitamin E isoforms have not been characterized. In the present study, we investigated the effects of six different isoforms of vitamin E on the ischemic brain damage in the mice middle cerebral artery (MCA) occlusion model. All vitamin E isoforms were injected i.v., twice, immediately before and 3 h after the occlusion. .alpha.-tocopherol (2 mM), .alpha.-tocotrienol (0.2 and 2 mM) and .gamma.-tocopherol (0.2 and 2 mM) significantly decreased the size of the cerebral infarcts 1 day after the MCA occlusion, while .gamma.-tocotrienol, .delta.-tocopherol and .delta.-tocotrienol showed no effect on the cerebral infarcts. These results suggest that .alpha.-tocotrienol and .gamma.-tocopherol are potent and effective agents for preventing cerebral infarction induced by MCA occlusion. .COPYRGT. 2002 Elsevier Science Ireland Ltd. All rights reserved.

L108 ANSWER 10 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002281297 EMBASE
TITLE: The nitration product 5-nitro-.gamma.-tocopherol is increased in the Alzheimer brain.
AUTHOR: Williamson K.S.; Gabbita S.P.; Mou S.; West M.; Pye Q.N.; Markesbery W.R.; Cooney R.V.; Grammas P.; Reimann-Philipp U.; Floyd R.A.; Hensley K.
CORPORATE SOURCE: K. Hensley, Free Radical Biol./Aging Res. Prog., Oklahoma Medical Research Foundation, 25 NE 13th Street, Oklahoma City, OK 73104, United States. Kenneth-

Hensley@omrf.ouhsc.edu
SOURCE: Nitric Oxide - Biology and Chemistry, (2002) 6/2 (221-227).
Refs: 28
ISSN: 1089-8603 CODEN: NIOXF5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Oxidative stress and quasi-inflammatory processes recently have been recognized as contributing factors in the pathogenesis of Alzheimer's disease (AD). Reactive nitrating species have specifically been implicated in AD based on immunochemical and instrumental detection of nitrotyrosine in AD brain protein. The significance of lipid-phase nitration has not been investigated in AD. This study documents a significant two- to threefold increase in the lipid nitration product 5-nitro-.gamma.-tocopherol in affected regions of the AD brain as determined by high-performance liquid chromatography with electrochemical detection. In a bioassay to compare the relative potency of .alpha.-tocopherol and .gamma.-tocopherol against nitrative stress, rat brain mitochondria were exposed to the peroxynitrite-generating compound SIN-1. The oxidation-sensitive Kreb's cycle enzyme .alpha.-ketoglutarate dehydrogenase was inactivated by SIN-1, in a manner that could be significantly attenuated by .gamma.-tocopherol (at <10 .mu.M) but not by .alpha.-tocopherol. These data indicate that nitric oxide-derived species are significant contributors to lipid oxidation in the AD brain. The findings are discussed in reference to the neuroinflammatory hypothesis of AD and the possible role of .gamma.-tocopherol as a major lipid-phase scavenger of reactive nitrogen species. .COPYRGT. 2001 Elsevier Science (USA).

L108 ANSWER 11 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96338884 EMBASE
DOCUMENT NUMBER: 1996338884
TITLE: Magnetic resonance imaging white matter hyperintensities in clinically normal elderly individuals: Correlations with plasma concentrations of naturally occurring antioxidants.
AUTHOR: Schmidt R.; Hayn M.; Fazekas F.; Kapeller P.; Esterbauer H.
CORPORATE SOURCE: Department of Neurology, Karl-Franzens University Graz, Auenbruggerplatz 22,A-8036 Graz, Austria
SOURCE: Stroke, (1996) 27/11 (2043-2047).
ISSN: 0039-2499 CODEN: SJCCA7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background and Purpose: While mailer hyperintensities are a common magnetic resonance imaging (MRI) observation in the elderly. They are believed to represent a subclinical form of ischemic brain damage, but the underlying pathophysiological mechanisms are still incompletely understood. We postulated that oxidative mechanisms may favor the development of these changes and therefore correlated their presence and extent with the plasma concentrations of 10 naturally occurring antioxidants. Methods: We studied 355 clinically normal volunteers 45 to 75 years of age who were randomly selected from the official community register. A 1.5-T MRI of the brain and measurements of the plasma concentrations of antioxidants including zeaxanthin, cryptoxanthin, canthaxanthin, lycopene, alpha- and betacarotene, retinol, gamma and alpha-tocopherol, as well as ascorbate were performed in all study participants. White matter hyperintensities were graded as punctate, beginning confluent, and confluent abnormalities. Results: Punctate,

beginning confluent, and confluent white matter abnormalities occurred in 101 (28.5%), 44 (12.4%), and 14 (3.9%) individuals, respectively. Study participants with white matter damage were significantly older and had a higher frequency of arterial hypertension and cardiac disease but lower serum concentrations of total cholesterol. The plasma levels of lycopene and alpha-tocopherol were significantly lower in subjects with early confluent and confluent white matter hyperintensities, while individuals with punctate foci had an antioxidant status similar to those with normal MRI scans. Alpha- tocopherol was the only antioxidant that remained significantly and inversely related to the presence of beginning confluent and confluent white matter changes after adjustment for the between-group differences in age, arterial hypertension, cardiac disease, and cholesterol. The adjusted odds ratio for early confluent and confluent white matter abnormalities was 3.70 (95% CI, 1.69 to 8.10) in the lowest compared with the highest quartile of the alpha- tocopherol concentration. The odds ratio increased to 7.11 (95% CI, 1.63 to 22.84) when quintiles of the alpha-tocopherol level were compared. Conclusions: These data do not prove a causal relation, but they provide evidence of an association between low plasma concentrations of vitamin E and a higher risk of cerebral white matter disease in elderly normal subjects.

L108 ANSWER 12 OF 25 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-599368 [64] WPIDS
DOC. NO. CPI: C2002-169201
TITLE: Preparation of cis-isomer of 4-benzoylamino **chroman derivatives** useful for treating e.g. epilepsy involves synthesis of corresponding cis-amine compound and acylating the compound.
DERWENT CLASS: B02
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM PLC; (EVAN-I) EVANS J M; (GEEN-I) GEEN G R; (MANN-I) MANN I S; (THOM-I) THOMPSON M
COUNTRY COUNT: 98
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002042285	A1	20020530	(200264)*	EN	32

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2002023852 A 20020603 (200264)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002042285	A1	WO 2001-GB5133	20011121
AU 2002023852	A	AU 2002-23852	20011121

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002023852	A Based on	WO 200242285

PRIORITY APPLN. INFO: GB 2000-28697 20001123
AB WO 200242285 A UPAB: 20021007
NOVELTY - Preparation of cis-isomer of 4-benzoylamino **chroman derivatives** involves reacting a corresponding cis-amine isomer with an acylating agent.

DETAILED DESCRIPTION - Preparation of cis-isomer of 4-benzoylamino **chroman derivatives** of formula (I), their salts or solvate involves reacting a cis-isomer of a compound of formula (III) or its salt with an acylating agent of formula R7COL.

Y = N or C-R1;

R1 R2 = one is T, the other is H; or

R1 R2 = one is NO2, CN or 1-3C alkylcarbonyl and the other is methoxy or amino substituted by 1-2 1-6C alkyl or 2-7C alkanoyl;

T = 3-8C cycloalkyl, 1-6C alkyl optionally interrupted by O or substituted by OH, 1-6C alkoxy or substituted amino carbonyl, 1-6C alkylcarbonyl, 1-6C alkoxycarbonyl, 1-6C alkylcarbonyloxy, 1-6C alkoxy, nitro, cyano, halo, trifluoromethyl, CF3S, CF3-A-, CF2H-A', trifluoromethoxy, 1-6C alkylsulfinyl, perfluoro(2-6C)alkylsulfonyl, 1-6C alkylsulfonyl, 1-6C alkoxysulfinyl, 1-6C alkoxysulfonyl, (hetero)aryl, arylcarbonyl, heteroarylcarbonyl, phosphono, arylcarbonyloxy, heteroarylcarbonyloxy, arylsulfinyl, heteroarylsulfinyl, arylsulfonyl, heteroarylsulfonyl (where aromatic moiety is optionally substituted), 1-6C alkylcarbonylamino, 1-6C alkoxycarbonylamino, 1-6C alkyl-thiocarbonyl, 1-6C alkoxy-thiocarbonyl, 1-6C alkyl-thiocarbonyloxy, 1-mercapto 2-7C alkyl, formyl, aminosulfinyl, aminosulfonyl, aminocarbonyl (where amino is optionally mono or di substituted by 1-6C alkyl), 1-6C alkylsulfinylamino, 1-6C alkylsulfonylamino, 1-6C alkoxysulfinylamino, 1-6C alkoxysulfonylamino, ethylenyl (terminally substituted by 1-6C alkylcarbonyl, nitro or cyano), -C(1-6C alkyl)NOH or -C(1-6C alkyl)NNH2;

R1+R2 = -(CH2)4- or -CH=CH-CH=CH-, optionally substituted triazole or oxadiazole ring;

A = -CF2-, -CO-, -CH2-, CH(OH), SO2, SO, CH2O or CONH;

A' = O, S, SO, SO2, CF2 or CFH;

R3 and R4 = H or T3;

T3 = 1-4C alkyl, CF3 or CH2Xa, carbonyl;

Xa = halo, 1-4C alkoxy, hydroxy, 1-4C alkylcarbonyloxy, -S-(1-4C)alkyl, nitro, amino (optionally mono or di substituted by 1-4C alkyl), cyano or 1-4C alkoxycarbonyl;

R3+R4 = 2-5C polymethylene optionally substituted by 1-4C alkyl;

R5 = T' or hydroxy;

T' = 1-6C alkylcarbonyloxy, ONO2, benzyloxy, phenyloxy or 1-6C alkoxy;

R6 = H or 1-2C alkyl;

R9 = H;

R7 = heteroaryl or phenyl (both optionally substituted by T4);

T4 = halo, nitro, amino (optionally mono or di substituted by 1-4C alkyl), cyano, azido, 1-4C alkyl, 1-4C alkoxy, trifluoromethoxy or trifluoromethyl;

L = leaving group such as Cl;

X = O or NR10;

R10 = H or 1-6C alkyl.

provided that 1) either one of R1 and R2 is H and the other is T; 2) one of R3 and R4 is H or 1-4C alkyl and the other is T3; 3) when one or R1 and R2 is nitro, cyano or 1-3C alkylcarbonyl, the other is methoxy or amino optionally mono- or di-substituted by 1-6C alkyl or 2-7C alkanoyl; 4) when Y is N, R2 is H; 5) when R5 is T' then R6 is H and when R5 is hydroxy, R6 is H or 1-2C alkyl; and 6) HN-CO-R7 is cis to the R5 group.

INDEPENDENT CLAIMS are also included for:

(1) a compound of formula (V), provided that when Y is C-R1 then R1 is not cyano;

(2) compounds of formula (IX) and (VIII);

(3) 8-Acetyl-2-(3-methyl)-3a,9b-dihydro-4,4-dimethyl-(2H-1)benzopyrano(4,3-d)oxazole; and

(4) preparation of (III), (IX), (V) and (VIII).

R11 = 1-10C alkyl or 3-8C cycloalkyl optionally mono or di-substituted by halo, nitro, amino, hydroxy or cyano; and

R12 = hydroxy, 1-4C alkoxy or halogen.

ACTIVITY - Tranquilizer; Antidepressant; Neuroprotective;

Antiaddictive; Antiparkinsonian; Antimigraine; Cerebroprotective; Nootropic; Neuroleptic; Anticonvulsant; Vasotropic.

MECHANISM OF ACTION - None given.

USE - For preparation of 4-benzoylamino chroman derivatives (claimed) useful for treating epilepsy, anxiety, mania, depression, disorders associated with subarachnoid haemorrhage or neural shock, effects associated with withdrawal from substances of abuse, Parkinson's disease, psychosis, migraine with or without aura, cerebral ischemia, Alzheimer's disease, schizophrenia, obsessive compulsive disorder, panic and aggression.

ADVANTAGE - The method includes a shorter synthetic pathway, provides improved yields and reduces material costs. The method is suitable for use in stereospecific synthesis as no scrambling of the chiral centers occurs. Dwg.0/0

P
ischemia

L108 ANSWER 13 OF 25 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-102672 [11] WPIDS
DOC. NO. CPI: C2001-030051
TITLE: New **chroman derivatives** (I), their salts or in vivo-hydrolyzable esters, amides or carbamates, are useful for treating neurological disorders e.g. Alzheimer's disease, Parkinson's disease and AIDS-related dementia.
DERWENT CLASS: B02
INVENTOR(S): CHEN, D W C; FORST, J M
PATENT ASSIGNEE(S): (ASTR) ASTRAZENECA UK LTD
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000078742	A1	20001228	(200111)*	EN	52
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000054141	A	20010109	(200122)		
EP 1192146	A1	20020403	(200230)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2003502415	W	20030121	(200308)		67

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000078742	A1	WO 2000-GB2304	20000614
AU 2000054141	A	AU 2000-54141	20000614
EP 1192146	A1	EP 2000-938917	20000614
		WO 2000-GB2304	20000614
JP 2003502415	W	WO 2000-GB2304	20000614
		JP 2001-504908	20000614

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000054141	A	Based on	WO 200078742
EP 1192146	A1	Based on	WO 200078742
JP 2003502415	W	Based on	WO 200078742

PRIORITY APPLN. INFO: GB 1999-14025 19990617
AB WO 200078742 A UPAB: 20010224
NOVELTY - **Chroman derivatives** (I), their salts or in vivo-hydrolyzable esters, amides or carbamates, are new.

DETAILED DESCRIPTION - **Chroman derivatives** of formula (I), their salts or in vivo-hydrolyzable esters, amides or carbamates, are new.

R1 = H, 1-6C alkyl, 2-6C alkenyl or 2-6C alkynyl;

R2, R3 = H, or 1-6C alkyl, 2-6C alkenyl or 2-6C alkynyl (all optionally substituted by at least one X and/or Y), aryl, a carbon linked heteroaryl or heterocycle, or 3-12C cycloalkyl (optionally fused to a benzene ring);

X = halo, NO2, OH, 1-6C alkoxy, CN, amino, CF3, OCF3, carboxy, carbamoyl, mercapto, sulfamoyl, mesyl, N-1-6C alkylamino, N,N-(1-6C alkyl)2amino, 1-6C alkoxycarbonyl, N-1-6 C alkylcarbamoyl or N,N-(1-6C alkyl)2carbamoyl;

Y = aryl, a carbon linked heteroaryl or heterocycle or 3-12C cycloalkyl (optionally fused to a benzene ring) (all optionally substituted on a ring carbon by at least one Z; and -NH- containing heteroaryl and heterocycle may be optionally N-substituted by 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl or phenyl-1-6C alkyl);

Z = halo, NO2, OH, CN, amino, CF3, OCF3, carboxy, carbamoyl, mercapto, sulfamoyl, 1-6C alkyl, 2-6C alkenyl or 2-6C alkynyl, 1-6C alkoxy, 1-6C alkanoyl, 1-6C alkanoyloxy, N-1-6C alkylamino, N,N-(1-6C alkyl)2amino, 1-6C alkanoylamino, N-1-6 C alkylcarbamoyl or N,N-(1-6C alkyl)2carbamoyl, 1-6C alkylS(O)a, 1-6C alkoxycarbonyl, N-1-6C alkylsulfamoyl, N,N-(1-6C alkyl)2sulfamoyl or phenyl 1-6C alkyl; or

NR2R3 = heterocyclic or heteroaryl ring (both optionally substituted on a ring carbon by Z; and -NH- containing heteroaryl and heterocycle may be optionally N-substituted by 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl or 1-6C alkylsulfonyl);

a = 0-2;

R4 = halo, OH, 1-6C alkyl, 1-6C alkoxy, halo-1-6C alkyl, CN, NO2 or 2-6C alkenyl;

R5 = 1-6C alkyl;

n = 1-2;

r = 0-4; and

s = 0-3;

provided that if r =1, R4 = 6-linked cyano moiety, s = 3, R5 = 2-linked methyl, n = 1, and R1, R2 = H, then R3 is not phenyl or benzyl; if r, s = 0, R1 = H, and n = 2, R1, R2 are not both ethyl or not both H (sic); or if r, s = 0, R1 = H, and n = 1, R1, R2 are not both ethyl.

An INDEPENDENT CLAIM is included for preparations of (I).

ACTIVITY - **Neuroprotective**; nootropic; antiparkinsonian; anti-HIV; vasotropic; antidiabetic.

MECHANISM OF ACTION - (I) binds to the (3H)-emopamil binding site.

Methods for the (3H)-emopamil binding to guinea pig liver membranes, 3H-D-388 binding to rat brain cortical membranes, gerbil global model of **cerebral ischemia** and transient focal ischemia in rats are disclosed. IC50 for (S)-chroman-4-yl-(2-(1,3-dihydroisoindol-2-yl)ethyl)methylamine (I') for (3H)-emopamil binding to guinea pig liver membranes was 68 nM.

USE - (I) are useful in the treatment of **stroke**, head trauma, transient **cerebral ischemic** attack, and chronic neurodegenerative disorders e.g. Alzheimer's disease, Parkinson's disease, diabetic neuropathy, amyotrophic lateral sclerosis, multiple sclerosis and AIDS-related dementia (claimed).

ADVANTAGE - (I) are selective towards the (3H)-emopamil binding site without directly acting at neuronal voltage-sensitive calcium channels (VSCC) or N-methyl-D-aspartate (NMDA) receptors.

Dwg.0/0

L108 ANSWER 14 OF 25 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2001-102663 [11] WPIDS
DOC. NO. CPI: C2001-030042
TITLE: 4-(Aminopiperidinyl)tetrahydro -naphthalene, -chroman and -thiochroman derivatives used for treating e.g. head trauma, **stroke**, Alzheimer's and Parkinson's diseases, multiple sclerosis, dementia and diabetic neuropathy.
DERWENT CLASS: B02 B03
INVENTOR(S): MCLAREN, C D; SIMON-BIERENBAUM, R E; WARAWA, E J
PATENT ASSIGNEE(S): (ASTR) ASTRAZENECA UK LTD
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000078718	A1	20001228	(200111)*	EN	45
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000054142	A	20010109	(200122)		
EP 1204641	A1	20020515	(200239)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2003502404	W	20030121	(200308)		57

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000078718	A1	WO 2000-GB2306	20000614
AU 2000054142	A	AU 2000-54142	20000614
EP 1204641	A1	EP 2000-938919	20000614
		WO 2000-GB2306	20000614
JP 2003502404	W	WO 2000-GB2306	20000614
		JP 2001-504885	20000614

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000054142	A	Based on	WO 200078718
EP 1204641	A1	Based on	WO 200078718
JP 2003502404	W	Based on	WO 200078718

PRIORITY APPLN. INFO: GB 1999-14024 19990617
AB WO 200078718 A UPAB: 20010224
NOVELTY - 4-(Aminopiperidinyl)tetrahydro -naphthalene, -chroman and -thiochroman derivatives (I) are new.

DETAILED DESCRIPTION - 4-(Aminopiperidyl)tetrahydro -naphthalene, -chroman and -thiochroman derivatives of formula (I) and their salts and in vivo hydrolyzable esters, amides and carbamates new.

X = CH2, O, or S;

R1, R2 = H, or 1-6C alkyl, 3-6C alkenyl or 3-6C alkynyl (all optionally substituted by at least one halo, NO2, OH, 1-6C alkoxy, CN, amino, CF3, OCF3, COOH, carbamoyl, mercapto, sulfamoyl, mesyl, N-1-6C alkylamino, N,N-(1-6C alkyl)2amino, 1-6C alkoxycarbonyl, N-1-6C alkylcarbamoyl, N,N-(1-6C alkyl)2carbamoyl or a group of formula B-(CH2)q), or

NR1R2 = heterocyclyl or heteroaryl (both optionally C-substituted by at least one halo, NO2, CN, OH, CF3, OCF3, amino, COOH, carbamoyl,

mercapto, sulfamoyl, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-6C alkoxy, 1-6C alkanoyl, 1-6C alkanoyloxy, N-1-6C alkylamino, N,N-(1-6C alkyl)2amino, 1-6C alkanoylamino, N-1-6C alkylcarbamoyl, N,N-(1-6C alkyl)2carbamoyl, 1-6C alkylS(O)a, 1-6C alkoxycarbonyl, N-1-6C alkylsulfamoyl, N,N-(1-6C alkyl)2sulfamoyl or phenyl 1-6C alkyl, and when the ring contains NH, both are optionally N-substituted by 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-6C alkanoyl or 1-6C alkylsulfonyl);

B = 3-12C cycloalkyl optionally fused to a benzene ring or aryl, C-linked heteroaryl, C-linked heterocyclyl (all optionally substituted by at least halo, NO2 CN, OH, CF3, OCF3, amino, COOH, carbamoyl, mercapto, sulfamoyl, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-6C alkoxy, 1-6C alkanoyl, 1-6C alkanoyloxy, N-1-6C alkylamino, N,N-(1-6C alkyl)2amino, 1-6C alkanoylamino, N-1-6C alkylcarbamoyl, N,N-(1-6C alkyl)2carbamoyl, 1-6C alkylS(O)a, 1-6C alkoxycarbonyl, N-(1-6C alkyl)sulfamoyl, N,N-(1-6C alkyl)2sulfamoyl or phenyl 1-6C alkyl, and when heterocyclyl or heteroaryl ring contains NH, both are optionally N-substituted by 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-6C alkanoyl or 1-6C alkylsulfonyl);

R3 = halo, nitro, hydroxy, 1-6C alkoxy, cyano, NO2 or 2-6C alkenyl;

q = 0-6;

a = 0-2;

r = 0-4 and

s = 0-3.

An INDEPENDENT CLAIM is also included for the preparation of (I).

ACTIVITY - **Neuroprotective**; cerebroprotective; nootropic.

MECHANISM OF ACTION - (3H)-Emopamil binding site inhibitor.

In a (3H)-emopamil binding to guinea pig liver membrane test, 4-N-n-propylamino-1-(3,4-dihydro-2H-benzothiopyran-4-yl)piperidine (Ia) exhibited an IC50 value of 17 nM.

USE - Useful in treatment of neurological disorders, particularly **stroke**, head trauma, transient **cerebral ischemia** and chronic degenerative disorders e.g. Alzheimer's and Parkinson's diseases, diabetic neuropathy, amyotrophic lateral sclerosis, multiple sclerosis, and AIDS related dementia.

ADVANTAGE - (I) Are more selective for the binding site, and without activity at the neuronal voltage sensitive calcium channel, sigma-1 binding site or NMDA sites and therefore cause fewer side effects e.g. hypotension.

Dwg.0/0

L108 ANSWER 15 OF 25 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1999-314208 [27] WPIDS
DOC. NO. CPI: C1999-093013
TITLE: Neuronal regeneration and neurodegenerative disease treatment with aminomethyl-**chroman derivatives**.
DERWENT CLASS: B02
INVENTOR(S): FAHRIG, T; GERLACH, I; HORVATH, E; JORK, R
PATENT ASSIGNEE(S): (FARB) BAYER AG; (FAHR-I) FAHRIG T; (GERL-I) GERLACH I; (HORV-I) HORVATH E; (JORK-I) JORK R
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 19751949	A1	19990527	(199927)*		6
WO 9926621	A1	19990603	(199929)	GE	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
ZA 9810668	A	19990831	(199939)		17

AU 9916685 A 19990615 (199944)
NO 2000002638 A 20000523 (200045)
EP 1051170 A1 20001115 (200059) GE
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI
CN 1279604 A 20010110 (200128)
US 6235774 B1 20010522 (200130)
HU 2000004369 A2 20010428 (200131)
US 2001018530 A1 20010830 (200151)
KR 2001032357 A 20010416 (200163)
EP 1051170 B1 20011010 (200167) GE
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI
MX 2000005054 A1 20010201 (200168)
DE 59801724 G 20011115 (200176)
JP 2001523716 W 20011127 (200204) 17
US 6331561 B2 20011218 (200205)
NZ 504656 A 20020201 (200214)
ES 2164465 T3 20020216 (200222)
AU 745759 B 20020328 (200235)

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
DE 19751949	A1		DE 1997-19751949	19971124
WO 9926621	A1		WO 1998-EP7197	19981111
ZA 9810668	A		ZA 1998-10668	19981123
AU 9916685	A		AU 1999-16685	19981111
NO 2000002638	A		WO 1998-EP7197	19981111
			NO 2000-2638	20000523
EP 1051170	A1		EP 1998-961174	19981111
			WO 1998-EP7197	19981111
CN 1279604	A		CN 1998-811445	19981111
US 6235774	B1		WO 1998-EP7197	19981111
			US 2000-554971	20000523
HU 2000004369	A2		WO 1998-EP7197	19981111
			HU 2000-4369	19981111
US 2001018530	A1	Cont of	US 2000-554971	20000523
			US 2001-803621	20010309
KR 2001032357	A		KR 2000-705593	20000523
EP 1051170	B1		EP 1998-961174	19981111
			WO 1998-EP7197	19981111
MX 2000005054	A1		MX 2000-5054	20000523
DE 59801724	G		DE 1998-501724	19981111
			EP 1998-961174	19981111
			WO 1998-EP7197	19981111
JP 2001523716	W		WO 1998-EP7197	19981111
			JP 2000-521823	19981111
US 6331561	B2	Cont of	US 2000-554971	20000523
			US 2001-803621	20010309
NZ 504656	A		NZ 1998-504656	19981111
			WO 1998-EP7197	19981111
ES 2164465	T3		EP 1998-961174	19981111
AU 745759	B		AU 1999-16685	19981111

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9916685	A	Based on	WO 9926621
EP 1051170	A1	Based on	WO 9926621
US 6235774	B1	Based on	WO 9926621
HU 2000004369	A2	Based on	WO 9926621
US 2001018530	A1	Cont of	US 6235774

EP 1051170	B1	Based on	WO 9926621
DE 59801724	G	Based on	EP 1051170
		Based on	WO 9926621
JP 2001523716	W	Based on	WO 9926621
NZ 504656	A	Based on	WO 9926621
ES 2164465	T3	Based on	EP 1051170
AU 745759	B	Previous Publ.	AU 9916685
		Based on	WO 9926621

PRIORITY APPLN. INFO: DE 1997-19751949 19971124

AB DE 19751949 A UPAB: 19990714

NOVELTY - The use of 2-(substituted alkylaminomethyl)-chromans (I) for treating neurodegenerative disease and causing neuronal regeneration is new.

DETAILED DESCRIPTION - The use of aminomethyl-chromans of formula (I) or their optical isomers (specifically the (-)-enantiomers) or salts is claimed for the preparation of a medicament for treating neurodegenerative diseases and causing neuronal regeneration.

R1 = H;

R2 = H, OH, OMe, OEt, isopropoxy or OCH2C(Me)2Cl;

or R1+R2 = -CH2C(Me)2O-;

R3 = 5-8C cycloalkyl or o-benzosulfimidyl;

n = 1-5.

ACTIVITY - **Neuroprotective**; neuronal regeneration promotion. (I) reduce the formation of glial scar tissue in vivo. 2-(N-(4-(o-Benzosulfimidyl)butyl)-aminomethyl)-chroman (Ia) (as the (-)-enantiomer) was tested in the medial cerebral artery occlusion-induced **cerebral ischemia** model in mice. (Ia) was administered intravenously 2 and 4 hours after the operation, and the reduction of expression of glial fibrillary acidic protein (GFAP) in the brain was determined 7 days after the operation. The GFAP immunoreactivity (compared with that in untreated controls) at various doses of (Ia) was 94.0% at 1 mu g/kg, 79.7% at 10 mu g/kg, 62.3% at 30 mu g/kg and 59.5% at approx. 100 mg/kg. Administration of (Ia) during the acute phase of the disease thus gave a dose-dependent reduction of ischemia-induced GFAP immuoreactivity (and thus glial scar formation) in the chronic phase.

MECHANISM OF ACTION - Glial fibrillary acidic protein (GFAP) expression inhibitor.

USE - Especially for the regenerative treatment of neurological states resulting from damage by surgery, infection, implantation, exposure to toxic agents, tumors, nutritional deficiency, metabolic disease, Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis, epilepsy, drug abuse or addiction, bone marrow disease or damage, dystrophy or degeneration of the neural retina or peripheral neuropathy; or for the treatment of Alzheimer's disease in combination with surgical implants and/or prostheses (all claimed). (I) have previously been used in the treatment of the acute phase of **cerebral infarction**, **stroke** and **cerebral ischemia** (see EP352613-A, EP540914-A and EP749970-A), and have now been found to be effective in treatment of the post-acute phase of cerebral disorders or in treatment of chronic neurological diseases.

Dwg.0/0

L108 ANSWER 16 OF 25 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1997-044790 [05] WPIDS

DOC. NO. CPI: C1997-014346

TITLE: New (((di oxido-oxo-benzisothiazolyl)alkyl)aminomethyl) **chroman derivs**. - having strong affinity for 5-HT-1 receptors, used for treating CNS disorders (anxiety, stress, addiction etc.), pain etc. and esp. **stroke**.

DERWENT CLASS: B02

INVENTOR(S): FRIEDL, A; GLASER, T; HEINE, H; HORVATH, E; JORK, R;

KANHAI, W; SCHOHE-LOOP, R; SCHUHMACHER, J; SEIDEL, P;
YORK, R; BERGISCH, A F; SCHUMACHER, J; HORVATCH, E
PATENT ASSIGNEE(S): (FARB) BAYER AG
COUNTRY COUNT: 32
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 749970	A1	19961227	(199705)*	GE	27
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
DE 19522088	A1	19970102	(199706)		20
NO 9602579	A	19961220	(199709)		
AU 9655938	A	19970109	(199710)		
JP 09003068	A	19970107	(199711)		16
CA 2179205	A	19961220	(199716)		
ZA 9605144	A	19970326	(199718)		41
KR 97001347	A	19970124	(199803)		
SG 47153	A1	19980320	(199818)		
NZ 286824	A	19980826	(199840)		
HU 9601680	A2	19980728	(199842)		
AU 706755	B	19990624	(199936)		
US 5942529	A	19990824	(199941)		
NO 306064	B1	19990913	(199944)		
CN 1143079	A	19970219	(200059)		
IL 118672	A	20001031	(200059)		
EP 749970	B1	20010117	(200105)	GE	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
DE 59606332	G	20010222	(200118)		
ES 2155152	T3	20010501	(200136)		
MX 197761	B	20000727	(200160)		
TW 481665	A	20020401	(200309)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 749970	A1	EP 1996-109134	19960607
DE 19522088	A1	DE 1995-19522088	19950619
NO 9602579	A	NO 1996-2579	19960618
AU 9655938	A	AU 1996-55938	19960612
JP 09003068	A	JP 1996-177061	19960617
CA 2179205	A	CA 1996-2179205	19960614
ZA 9605144	A	ZA 1996-5144	19960618
KR 97001347	A	KR 1996-21954	19960618
SG 47153	A1	SG 1996-10068	19960614
NZ 286824	A	NZ 1996-286824	19960614
HU 9601680	A2	HU 1996-1680	19960618
AU 706755	B	AU 1996-55938	19960612
US 5942529	A	US 1996-663398	19960613
NO 306064	B1	NO 1996-2579	19960618
CN 1143079	A	CN 1996-108212	19960619
IL 118672	A	IL 1996-118672	19960617
EP 749970	B1	EP 1996-109134	19960607
DE 59606332	G	DE 1996-506332	19960607
		EP 1996-109134	19960607
ES 2155152	T3	EP 1996-109134	19960607
MX 197761	B	MX 1996-2383	19960618
TW 481665	A	TW 1996-106930	19960610

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 706755	B	Previous Publ.	AU 9655938
NO 306064	B1	Previous Publ.	NO 9602579
DE 59606332	G	Based on	EP 749970
ES 2155152	T3	Based on	EP 749970

PRIORITY APPLN. INFO: DE 1995-19522088 19950619

AB EP 749970 A UPAB: 19981021
2-(N-(1,1-Dioxido-3-oxo-2,3-dihydrobenzisothiazol-2-ylalkyl)-aminomethyl)-8-alkoxychroman derivs. of formula (I) and their isomers and salts are new. Q = benzisothiazolyl gp. of formula (i); R1 = H; R2 = CHMe2 or CH2CMe2Cl; or R1+R2 = CH2CMe2; a = 3-5 (pref. 3 or esp. 4).

USE - (I) are drugs with high activity for cerebral 5-HT1 receptors, and are useful for treating disorders of the serotoninergic system. They are used for treating CNS disorders, including anxiety, tension, depression or CNS-related sexual or sleeping disorders; regulating pathological uptake disorders associated with food , flavourant or addictive drugs; combatting cognitive deficiency, improving learning and memory performance and treating Alzheimer's disease; regulating the cardiovascular system and cerebral blood flow, including in the treatment of migraine; treating and preventing the sequellae of **cerebral infarction** (apoplexy) such as **stroke** attacks, **cerebral ischaemia** and cranial-**cerebral** trauma; or treating pain and immune system disorders. (I) are esp. used for treating **stroke** (claimed).

Daily dose is 0.01-100 (pref. 1-50) mg/kg.

ADVANTAGE - (I) have high affinity for 5-HT1 receptors, typically having Ki 0.5-2.8 nM for 5-HT1 receptors and 0.5-1.8 nM for 5-HT1A receptors. They have lower dependence on liver enzymes of the CYP 2D6 type for their metabolism than known chromans, and are thus more stable in liver microsomes and less subject to first pass metabolism.

Dwg.0/0

L108 ANSWER 17 OF 25 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1995-036361 [05] WPIDS
DOC. NO. CPI: C1995-016295
TITLE: New ((N-(phenyl)alkyl)-amino-alkoxy)fluoro-**chroman derivs.** - have 5-HT1A receptor affinity, and are used to treat anxiety, schizophrenia and drug dependency.
DERWENT CLASS: B02
INVENTOR(S): KIMURA, T; KONTANI, T; NAITO, R; WANIBUCHI, F; YAMAGUCHI, T; YASUNAGA, T
PATENT ASSIGNEE(S): (YAMA) YAMANOUCHI PHARM CO LTD
COUNTRY COUNT: 53
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9429293	A1	19941222	(199505)*	JA	83
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE					
W: AU BB BG BR BY CA CN CZ FI GE HU JP KE KG KR KZ LK LV MD MG MN MW NO NZ PL PT RO RU SD SI SK TJ TT UA US UZ VN					
AU 9469361	A	19950103	(199522)		
JP 07501572	X	19950803	(199539)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9429293	A1	WO 1994-JP923	19940608
AU 9469361	A	AU 1994-69361	19940608
JP 07501572	X	WO 1994-JP923	19940608
		JP 1995-501572	19940608

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9469361	A	Based on	WO 9429293
JP 07501572	X	Based on	WO 9429293

PRIORITY APPLN. INFO: JP 1993-138580 19930610

AB WO 9429293 A UPAB: 19950207

Fluorochroman derivs. of formula (I) and their salts are new. The dotted line represents an opt. double bond and when the double bond is present, R5 is absent; R1 = alkyl, OH, alkylthio, NH2, mono- or di- alkylamino, alkanoylamino, CN, NO2, alkanoyloxy, alkanoyl, alkoxycarbonyl, halogen, alkoxy-alkoxy, alkoxy, or alkoxy substd. by R'; R' = benzene ring fused to a 5 or 6 membered heterocyclic ring contg. one or two oxygen atoms; R2, R3 = H or a gp. as defined for R1; or R2+R3 = -CH=CH-CH=CH-; or R1+R2 = -O-(CH2)q-, -O-(CH2)m-O- or -(CH2)n-; q = 2-4; m = 1-3; n = 2-6; R4 = H, lower alkyl or aralkyl; R5 = OH, NH2 or alkoxy; R6 = H or alkyl; or CR5R6 = CO; A = ethylene, opt. substd. by alkyl; B = 1-10C alkylene. All alkyl, alkoxy and alkanoyl gps. are lower; i.e they have 1-6C.

Also claimed are the cpds. 5-, 6-, and 7-fluoro-8-hydroxy-4-chromanone (II) (see 'Preparation').

USE - Cpds. (I) have a selective affinity for 5-HT1A receptors and are effective in the treatment of anxiety, manic-depression, schizophrenia, sexual function disorders, eating disorders, sleep disorders and drug dependency. They can be used for **stroke**, **cerebral ischaemia**, mental handicap, learning or memory difficulties, Alzheimer's disease, and tremors. They can also be used for circulation disorders such as high blood pressure, migraine and so on, or digestive disorders such as gastrointestinal obstruction.

Dose is 0.01-300mg/day orally.

ADVANTAGE - The cpds. have very low affinity to adrenalin-alpha1 receptors and so have reduced side effects.

Dwg.0/0

L108 ANSWER 18 OF 25 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1993-144839 [18] WPIDS
DOC. NO. CPI: C1993-064658
TITLE: New 2-aminomethyl-**chroman derivs.** bind to serotonin receptors - used to treat CNS disorders e.g. anxiety, Alzheimer's disease, **stroke**, **cerebral infarction**, pain, etc..
DERWENT CLASS: B02
INVENTOR(S): DOMPERT, W; GLASER, T; HEINE, H; JUNGE, B; SCHOHE-LOOP, R; SOMMERMEYER, H; VIKTOR, DE VRY J M; DE, VRY J M V; VIKTOR, D V J M; DE, VRY J V; SCHONE-LOOP, R
PATENT ASSIGNEE(S): (FARB) BAYER AG
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 4135474	A1	19930429	(199318)*		32
EP 540914	A1	19930512	(199319)	GE	56
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
AU 9226264	A	19930429	(199324)		
NO 9203975	A	19930429	(199326)		
CA 2081300	A	19930429	(199328)		
FI 9204847	A	19930429	(199328)		
HU 62875	T	19930628	(199332)		
CZ 9203225	A3	19930512	(199335)		
JP 05194473	A	19930803	(199335)		46

ZA 9208291	A	19930728 (199335)	101	
TW 207537	A	19930611 (199340)		
US 5318988	A	19940607 (199422)	27	
US 5468882	A	19951121 (199601)	26	
EP 540914	B1	19990602 (199926)	GE	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE				
DE 59209704	G	19990708 (199933)		
ES 2132105	T3	19990816 (199939)		
US 5962513	A	19991005 (199948)		
JP 3299321	B2	20020708 (200247)	46	

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
DE 4135474	A1		DE 1991-4135474	19911028
EP 540914	A1		EP 1992-117605	19921015
AU 9226264	A		AU 1992-26264	19921007
NO 9203975	A		NO 1992-3975	19921013
CA 2081300	A		CA 1992-2081300	19921023
FI 9204847	A		FI 1992-4847	19921026
HU 62875	T		HU 1992-3383	19921028
CZ 9203225	A3		CS 1992-3225	19921026
JP 05194473	A		JP 1992-312965	19921028
ZA 9208291	A		ZA 1992-8291	19921027
TW 207537	A		TW 1992-107544	19920924
US 5318988	A		US 1992-963203	19921019
US 5468882	A	Div ex	US 1992-963203	19921019
			US 1994-215995	19940322
EP 540914	B1		EP 1992-117605	19921015
DE 59209704	G		DE 1992-509704	19921015
			EP 1992-117605	19921015
ES 2132105	T3		EP 1992-117605	19921015
US 5962513	A	Div ex	US 1992-963203	19921019
		Div ex	US 1994-215995	19940322
		Div ex	US 1995-503793	19950718
			US 1996-631386	19960412
JP 3299321	B2		JP 1992-312965	19921028

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 5468882	A	Div ex	US 5318988
DE 59209704	G	Based on	EP 540914
ES 2132105	T3	Based on	EP 540914
US 5962513	A	Div ex	US 5318988
		Div ex	US 5468882
JP 3299321	B2	Previous Publ.	JP 05194473

PRIORITY APPLN. INFO: DE 1991-4135474 19911028

AB DE 4135474 A UPAB: 19931112

2-Aminomethyl-**chroman derivs**. of formula (I) and their isomers and salts are new.

In (I) A, B and D = H, halogen, CN, N3, NO2, CHF2, CF3, OCHF2, OCF3, OH, COOH, 1-8C alkyl, 2-8C alkenyl, 1-8C acyl, 2-8C alkoxycarbonyl, NR2R3, N(R4)LR5 or OR6, or B+D forms a 5- to 7-membered ring contg. 0-2 heteroatoms (S,N,O) and substd. by 0-2 oxo gps. and by 0-2 of 1-6C alkyl, 1-6C alkoxy, OH, 3-6C cycloalkyl, Ph, halogen, CN, NO2 and gem-tetramethylene or gem-pentamethylene; E = a direct bond or a 1-10C alkylene, 2-10C alkenylene or 2-10C alkynylene gp. opt. substd. by Ph; G = (a) a cyclic gp. substd. by 0-3 of halogen, OH, NO2, CN, CHF2, CF3, OCHF2, OCF3, 1-8C alkyl, 1-8C alkoxy, phenyl(1-8C)alkyl, phenoxy(1-8C)alkyl,

phenyl(1-8C)alkoxy and phenoxy(1-8C)alkoxy, where the cyclic gp. is 6-10C aryl, 5- to 7-membered (un)satd. C-bonded heterocyclyl (contg. 1-3 of N, O or S and opt. fused with a 6C carbocyclic ring), cycloalkyl or a 3-15C bridged bicyclic carbocyclic gp., or (b) 3,3-ethylenedioxycyclopentyl or 3,3-ethylenedioxycyclohexyl; R1 = H, 1-8C alkyl or E'-G'; E' and G' = gps. as defined for E and G respectively.

USE - (I) have high affinity for cerebral serotonin 5-HT, receptors and sigma receptors and may be used to treat CNS disorders, e.g. anxiety, stress, depression, sexual dysfunction, sleep **disorders**, eating **disorders**, **cognitive dysfunction**, Alzheimer's disease and psychoses e.g. schizophrenia and mania; to modulate the cardiovascular system; to treat cerebrovascular disorders such as migraine, **stroke** and **cerebral ischaemia**; to control pain; and to treat disorders of the immune system.

Dwg.0/0

L108 ANSWER 19 OF 25 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1993-144838 [18] WPIDS
DOC. NO. CPI: C1993-064657
TITLE: New tri aza spiro decanone-methyl **chroman derivs.** - which bind to 5-HT1 and dopamine D2 receptors to treat central nervous system disorders.
DERWENT CLASS: B02
INVENTOR(S): DOMPERT, W; GLASER, T; HEINE, H; SCHOHE-LOOP, R; SOMMERMEYER, H; VIKTOR, DE VRY J M; DE, VRY J M V; DE, VIKTOR V J M; SOMMERMAYER, H; SCHOE-LOOP, R
PATENT ASSIGNEE(S): (FARB) BAYER AG
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 4135473	A1	19930429	(199318)*		12
EP 539803	A1	19930505	(199318)	GE	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
AU 9226265	A	19930429	(199324)		
NO 9203974	A	19930429	(199326)		
CA 2081256	A	19930429	(199328)		
FI 9204848	A	19930429	(199328)		
ZA 9208290	A	19930728	(199335)		34
JP 05222040	A	19930831	(199339)		12
CZ 9203224	A3	19930714	(199340)		
TW 208010	A	19930621	(199341)		
HU 64068	T	19931129	(199401)		
AU 650792	B	19940630	(199430)		
EP 539803	B1	19990107	(199906)	GE	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
DE 59209607	G	19990218	(199913)		
ES 2125879	T3	19990316	(199918)		
US 6060482	A	20000509	(200030)		
JP 3257708	B2	20020218	(200219)		12

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 4135473	A1	DE 1991-4135473	19911028
EP 539803	A1	EP 1992-117606	19921015
AU 9226265	A	AU 1992-26265	19921007
NO 9203974	A	NO 1992-3974	19921013
CA 2081256	A	CA 1992-2081256	19921023
FI 9204848	A	FI 1992-4848	19921026
ZA 9208290	A	ZA 1992-8290	19921027

JP 05222040	A	JP 1992-312798	19921028
CZ 9203224	A3	CS 1992-3224	19921026
TW 208010	A	TW 1992-107641	19920926
HU 64068	T	HU 1992-3382	19921028
AU 650792	B	AU 1992-26265	19921007
EP 539803	B1	EP 1992-117606	19921015
DE 59209607	G	DE 1992-509607	19921015
		EP 1992-117606	19921015
ES 2125879	T3	EP 1992-117606	19921015
US 6060482	A	US 1992-963165	19921019
JP 3257708	B2	JP 1992-312798	19921028

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 650792	B	Previous Publ.	AU 9226265
DE 59209607	G	Based on	EP 539803
ES 2125879	T3	Based on	EP 539803
JP 3257708	B2	Previous Publ.	JP 05222040

PRIORITY APPLN. INFO: DE 1991-4135473 19911028

AB DE 4135473 A UPAB: 19931112

8-(2-Chromanylmethyl) -1,3,8-triazaspiro (4,5)decan-4-ones of formula (I) and their isomers and salts are new; where A, B and D = H, halogen, CN, N3, NO2, CHF2, CF3, OCHF2, OCF3, OH, COOH, 1-8C alkyl, 2-8C alkenyl, 1-8C acyl, 2-8C alkoxycarbonyl, NR3R4, N(R5)LR6 or OR7, or B+D forms a 5- to 7-membered ring contg. 0-2 heteroatoms (S,N,O) and substd. by 0-2 oxo gps. and by 0-2 of 1-6C alkyl, 1-6C alkoxy, OH, 3-6C cycloalkyl, Ph, halogen, CN, NO2 and gem-tetramethylene or gem-pentamethylene; R3-R5 = H, 1-8C alkyl, Ph or CH2Ph; L = CO or SO2; R6 = 1-8C alkyl, CH2Ph, or 6-10C aryl opt. substd. by halogen, OH, NO2, CN, CF3, OCF3, 1-6C alkyl or 1-6C alkoxy; R7 = 1-8C alkyl or 2-8C alkenyl, opt. substd. by 3-6C cycloalkyl or Ph; R1 and R2 = H, alkyl, or phenyl or benzyl substd. by 0-3 of halogen, OH, CN, CHF2, OCHF2, CF3, OCF3, 1-8C alkyl and 1-8C alkoxy.

USE - (I) have high affinity for cerebral serotonin 5-HT, receptors and dopamine D2 receptors. They may be used to treat CNS disorders, e.g. anxiety, stress, depression, sexual dysfunction, sleep **disorders**, eating **disorders**, **cognitive dysfunction**, Alzheimer's disease and psychoses such as schizophrenia and mania; to modulate the caridovascular system; to treat cerebrovascular disorders such as migraine, **stroke** and **cerebral ischaemia**; and to control pain.

Dwg.0/0

L108 ANSWER 20 OF 25 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1989-186598 [26] WPIDS
CROSS REFERENCE: 1991-024878 [04]
DOC. NO. CPI: C1989-082525
TITLE: New cyclohexadiene cpds. useful for treating cerebral insufficiency - are 4-(6-methyl-benzoquinonyl)-tetra hydro naphthalene,-chroman or -thia **chroman derivs**..
DERWENT CLASS: B02 B05
INVENTOR(S): MIYANO, S; SATOH, F; SUMOTO, K; SUZUKI, K; TATSUOKA, T
PATENT ASSIGNEE(S): (SUNR) SUNTORY LTD
COUNTRY COUNT: 18
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 322248	A	19890628	(198926)*	EN	59

R: AT BE CH DE ES FR GB GR IT LI LU NL SE

JP 01165538	A	19890629	(198932)		
JP 01197453	A	19890809	(198938)		
AU 8827422	A	19890629	(198939)		
JP 02069470	A	19900308	(199017)		
US 5057514	A	19911015	(199144)		
US 5179092	A	19930112	(199305)		24
EP 322248	B1	19930804	(199331)	EN	74
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
DE 3882956	G	19930909	(199337)		
US 5288752	A	19940222	(199408)		24
US 5292768	A	19940308	(199410)		24
CA 1327574	C	19940308	(199415)		
ES 2058315	T3	19941101	(199444)		
JP 2599413	B2	19970409	(199719)		10
JP 2710353	B2	19980210	(199811)		13
KR 9702518	B1	19970305	(199935)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 322248	A		EP 1988-312263	19881222
JP 01165538	A		JP 1987-322951	19871222
JP 01197453	A		JP 1988-21863	19880203
JP 02069470	A		JP 1988-220497	19880905
US 5057514	A		US 1988-286857	19881220
US 5179092	A	Div ex	US 1988-286857	19881220
			US 1991-737717	19910730
EP 322248	B1		EP 1988-312263	19881222
DE 3882956	G		DE 1988-3882956	19881222
			EP 1988-312263	19881222
US 5288752	A	Div ex	US 1988-286857	19881220
		Div ex	US 1991-737717	19910730
			US 1992-980238	19921123
US 5292768	A	Div ex	US 1988-286857	19881220
		Div ex	US 1991-737717	19910730
			US 1992-980207	19921123
CA 1327574	C		CA 1988-586699	19881221
ES 2058315	T3		EP 1988-312263	19881222
JP 2599413	B2		JP 1988-21863	19880203
JP 2710353	B2		JP 1988-220497	19880905
KR 9702518	B1		KR 1988-17223	19881222

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 5179092	A	Div ex	US 5057514
DE 3882956	G	Based on	EP 322248
US 5288752	A	Div ex	US 5057514
		Div ex	US 5179092
US 5292768	A	Div ex	US 5057514
		Div ex	US 5179092
ES 2058315	T3	Based on	EP 322248
JP 2599413	B2	Previous Publ.	JP 01197453
JP 2710353	B2	Previous Publ.	JP 02069470

PRIORITY APPLN. INFO: JP 1988-220497 19880905; JP 1987-322951 19871222; JP 1988-21863 19880203

AB EP 322248 A UPAB: 19980709

Cyclohexadiene derivs. of formula (I) and their salts are new. A = CH2, O or S; R1 = Me or OMe; R2 = OH or opt. esterified or amidated carboxy; R3 = H or lower alkyl; n = 0-6. Pref R1 = OMe; R2 = COR4; R4 = OH, Morpholino,

thiamorpholino, piperidino or N-Methylpiperazinyl.

USE - (I) are useful for treating cerebral insufficiency and the symptoms derived from **cerebral ischaemic** diseases e.g. **cerebral infarct** sequela, **cerebral** haemorrhage, sequela and cerebral arteriosclerosis sequela and various organic disorders derived from senile dementia, dementia presenilis, amnesia, cephalic traumatic sequela and cerebral operation sequela. They are also useful for treating diseases caused by cerabral hypoxia or anoxia. (I) have low toxicity. Dose is 0.1-1000 (pref. 10-500) mg/day. Dwg.0/0

L108 ANSWER 21 OF 25 USPATFULL
ACCESSION NUMBER: 2002:295219 USPATFULL
TITLE: Use of gamma-tocopherol and its oxidative metabolite LLU-alpha in the treatment of disease
INVENTOR(S): Wechter, William J., Ojai, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002165268	A1	20021107
	US 6555575	B2	20030429
APPLICATION INFO.:	US 2002-134140	A1	20020426 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-814330, filed on 21 Mar 2001, GRANTED, Pat. No. US 6410589 Continuation of Ser. No. US 1999-461645, filed on 14 Dec 1999, GRANTED, Pat. No. US 6242479 Continuation of Ser. No. US 1998-215608, filed on 17 Dec 1998, GRANTED, Pat. No. US 6048891
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: KNOBBE MARTENS OLSON & BEAR LLP, 620 NEWPORT CENTER DRIVE, SIXTEENTH FLOOR, NEWPORT BEACH, CA, 92660
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 1650
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is generally related to the discovery of the therapeutic benefit of administering .gamma.-tocopherol and .gamma.-tocopherol derivatives. More specifically, the use of .gamma.-tocopherol and racemic LLU-.alpha., (S)-LLU-.alpha., or .gamma.-tocopherol derivatives as antioxidants and nitrogen oxide scavengers which treat and prevent high blood pressure, thromboembolic disease, cardiovascular disease, cancer, natriuretic disease, the formation of neuropathological lesions, and a reduced immune system response are disclosed.

IT **178167-88-9P**
(.gamma.-tocopherol and oxidative metabolite LLU-.alpha. in treatment of natriuretic disease)

L108 ANSWER 22 OF 25 USPATFULL
ACCESSION NUMBER: 2001:182622 USPATFULL
TITLE: Use of gamma-tocopherol and its oxidative metabolite LLU-alpha in the treatment of disease
INVENTOR(S): Wechter, William J., Ojai, CA, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001031782	A1	20011018
	US 6410589	B2	20020625
APPLICATION INFO.:	US 2001-814330	A1	20010321 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1999-461645, filed on 14 Dec 1999, GRANTED, Pat. No. US 6242479 Continuation of

Ser. No. US 1998-215608, filed on 17 Dec 1998, GRANTED, Pat. No. US 6048891
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: KNOBBE MARTENS OLSON & BEAR LLP, 620 NEWPORT CENTER DRIVE, SIXTEENTH FLOOR, NEWPORT BEACH, CA, 92660
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
LINE COUNT: 1667
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is generally related to the discovery of the therapeutic benefit of administering .gamma.-tocopherol and .gamma.-tocopherol derivatives. More specifically, the use of .gamma.-tocopherol and racemic LLU-.alpha., (S)-LLU-.alpha., or .gamma.-tocopherol derivatives as antioxidants and nitrogen oxide scavengers which treat and prevent high blood pressure, thromboembolic disease, cardiovascular disease, cancer, natriuretic disease, the formation of neuropathological lesions, and a reduced immune system response are disclosed.
IT **178167-88-9P**
(.gamma.-tocopherol and oxidative metabolite LLU-.alpha. in treatment of natriuretic disease)

L108 ANSWER 23 OF 25 USPATFULL
ACCESSION NUMBER: 2001:82804 USPATFULL
TITLE: Use of .gamma.-tocopherol and its oxidative metabolite LLU-.alpha. in the treatment of disease
INVENTOR(S): Wechter, William J., Redlands, CA, United States
PATENT ASSIGNEE(S): Loma Linda University Medical Center, Loma Linda, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6242479	B1	20010605
APPLICATION INFO.:	US 1999-461645		19991214 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-215608, filed on 17 Dec 1998, now patented, Pat. No. US 6048891
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Henley, III, Raymond
LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear, LLP
NUMBER OF CLAIMS: 54
EXEMPLARY CLAIM: 1
LINE COUNT: 1803
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is generally related to the discovery of the therapeutic benefit of administering .gamma.-tocopherol and .gamma.-tocopherol derivatives. More specifically, the use of .gamma.-tocopherol and racemic LLU-.alpha., (S)-LLU-.alpha., or .gamma.-tocopherol derivatives as antioxidants and nitrogen oxide scavengers which treat and prevent high blood pressure, thromboembolic disease, cardiovascular disease, cancer, natriuretic disease, the formation of neuropathological lesions, and a reduced immune system response are disclosed.
IT **178167-88-9P**
(.gamma.-tocopherol and oxidative metabolite LLU-.alpha. in treatment of natriuretic disease)

L108 ANSWER 24 OF 25 USPATFULL
ACCESSION NUMBER: 2000:157451 USPATFULL
TITLE: Natriuretic compounds
INVENTOR(S): Wechter, William J., Redlands, CA, United States
Murray, David E., Redlands, CA, United States

Kantoci, Darko, Redlands, CA, United States
Levine, Barry H., Oakland, CA, United States
Benaksas, Elaine J., Yorba Linda, CA, United States
PATENT ASSIGNEE(S): Loma Linda University Medical Center, Loma Linda, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6150402		20001121
APPLICATION INFO.:	US 1994-290430		19940815 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Owens, Amelia
LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear, LLP.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 1509
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds, methods and compositions are provided for inducing natriuresis in a mammal. Methods for isolating and synthesizing the natriuretic compounds are also provided. Therapeutic methods using the natriuretic compounds are also provided. The natriuretic compounds are capable of inducing sodium excretion in a mammal without inducing corresponding prolongated potassium excretion.
IT **178167-88-9P**
(natriuretic cyclic compds. for stimulating sodium excretion in treatment of hypertension, heart diseases, and HIV infection)

L108 ANSWER 25 OF 25 USPATFULL
ACCESSION NUMBER: 2000:84320 USPATFULL
TITLE: Natriuretic compounds
INVENTOR(S): Wechter, William J., Redlands, CA, United States
Murray, David E., Redlands, CA, United States
Kantoci, Darko, Redlands, CA, United States
Levine, Barry H., Oakland, CA, United States
Benaksas, Elaine J., Yorba Linda, CA, United States
PATENT ASSIGNEE(S): Loma Linda University Medical, Loma Linda, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6083982		20000704
APPLICATION INFO.:	US 1998-57731		19980409 (9)

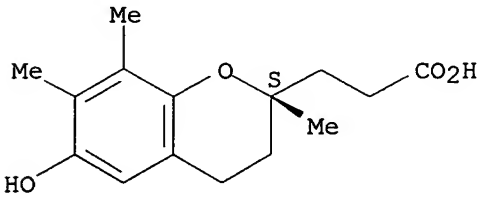
RELATED APPLN. INFO.: Division of Ser. No. US 1994-290430, filed on 15 Aug 1994
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Owens, Amelia
LEGAL REPRESENTATIVE: Knobble, Martens, Olson & Bear, LLP.
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 1557
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds, methods and compositions are provided for inducing natriuresis in a mammal. Methods for isolating and synthesizing the natriuretic compounds are also provided. Therapeutic methods using the natriuretic compounds are also provided. The natriuretic compounds are capable of inducing sodium excretion in a mammal without inducing corresponding prolonged potassium excretion.
IT **178167-88-9P**
(natriuretic cyclic compds. for stimulating sodium excretion in

treatment of hypertension, heart diseases, and HIV infection)

FILE 'HOME' ENTERED AT 13:07:54 ON 17 JUN 2003

ANSWER 1 OF 4 REGISTRY COPYRIGHT 2003 ACS
RN 178167-88-9 REGISTRY
CN 2H-1-Benzopyran-2-propanoic acid, 3,4-dihydro-6-hydroxy-2,7,8-trimethyl-, (2S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2H-1-Benzopyran-2-propanoic acid, 3,4-dihydro-6-hydroxy-2,7,8-trimethyl-, (S)-
OTHER NAMES:
CN **(S)-LLU-.alpha.**
CN **Natriuretic agent LLU-.alpha.**
CN **Natriuretic factor LLU-.alpha.**
FS STEREOSEARCH
DR 170427-25-5
MF C15 H20 O4
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

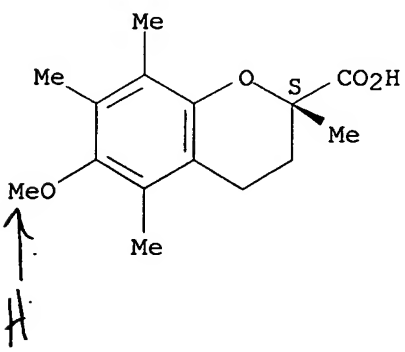
19 REFERENCES IN FILE CA (1957 TO DATE)
19 REFERENCES IN FILE CAPLUS (1957 TO DATE)

=> s trolox
L2 6 TROLOX

=> d l2

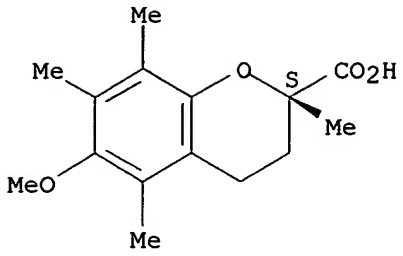
L2 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 135806-59-6 REGISTRY
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-6-methoxy-2,5,7,8-tetramethyl-, (2S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-6-methoxy-2,5,7,8-tetramethyl-, (S)-
OTHER NAMES:
CN **(S)-O-Methyltrolox**
CN **(S)-Trolox methyl ether**
FS STEREOSEARCH
MF C15 H20 O4
SR CA
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, CHEMCATS, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



= ∝ metabolite

408.654.5831



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

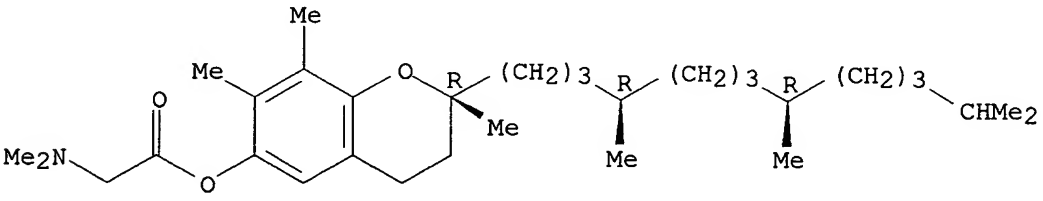
13 REFERENCES IN FILE CA (1957 TO DATE)
13 REFERENCES IN FILE CAPLUS (1957 TO DATE)

=> s tocopherol
L3 314 TOCOPHEROL

=> d l3

L3 ANSWER 1 OF 314 REGISTRY COPYRIGHT 2003 ACS
RN 521061-09-6 REGISTRY
CN Glycine, N,N-dimethyl-, (2R)-3,4-dihydro-2,7,8-trimethyl-2-[(4R,8R)-4,8,12-trimethyltridecyl]-2H-1-benzopyran-6-yl ester, hydrochloride (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **.gamma.-Tocopherol dimethylgycine ester hydrochloride**
FS STEREOSEARCH
MF C32 H55 N O3 . Cl H
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



● HCl

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

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